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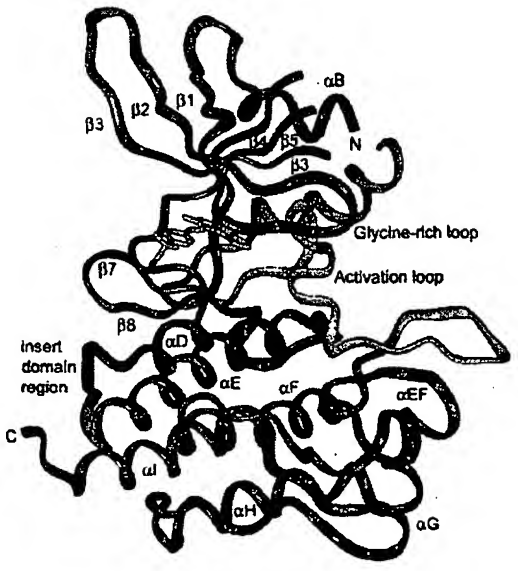
(54) Catalytic domains of the human hepatocyte growth factor receptor tyrosine kinase and methods for identification of inhibitors thereof

(57) The identification, isolation, purification, and characterization of the catalytic domain of the human hepatocyte growth factor receptor kinase (hHGFR) are described. A crystal structure of the hHGFR kinase domain is reported herein. This structure provides a three-dimensional description of the binding site of the hHGFR for structure-based design of small molecule inhibitors thereof as therapeutic agents. The kinase domain of human HGFR and its associated crystal structure is described for use in the discovery, identification and characterization of modulators of human HGFR.

Figure 2



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Description

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. provisional application Serial No. 60/277,968, filed March 23, 2001, which is hereby incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention generally relates to the isolation and purification of the catalytic domain of the human hepatocyte growth factor receptor kinase (the *Met* protooncogene product, *Met;* HGFR) and its use in the discovery, identification and characterization of inhibitors of same. The present invention further relates to the field of crystallography and, particularly, to X-ray crystallography data useful for identification and construction of therapeutic compounds in the treatment of various disease conditions associated with the *Met* receptor tyrosine kinase. More specifically, the invention relates to crystallized complexes of *Met.*

BACKGROUND OF THE INVENTION

[0003] Hepatocyte growth factor (HGF), also known as scatter factor, is a mesenchymally derived cytokine capable of inducing a variety of pleiotropic effects in normal and neoplastic cells (Sonnenberg et al., *J. Cell Biol.* 123:223-235 (1993); Matsumato et al., *Crit. Rev. Oncog.* 3:27-54 (1992); and Stoker et al., *Nature* 327:239-242 (1987)). These include proliferation of different types of epithelial and endothelial cells, dissociation of epithelial colonies into individual cells, stimulation of the motility (scattering) of epithelial cells, induction of epithelial morphogenesis (Montesano et al., *Cell* 67:901-908 (1991)), angiogenesis (Bussolino et al., *J. Cell Biol.* 119:629-641 (1992)), and promotion of the invasion of extracellular matrices (Stella et al., *Int J. Biochem. Cell Biol.* 12:1357-62 (1999)and Stuart et al., *Int J. Exp Path.* 81: 17-30 (2000)). *In vivo,* HGF is involved in tissue regeneration, tumor invasion, and embryonic processes, all of which are dependent on both cell motility and proliferation.

[0004] HGF initiates these physiologic processes through a high affinity receptor identified as the *c-Met* protooncogene product (Park et al., *Proc. Natl. Acad Sci USA* 84:6379-83 (1987); and Bottaro et al., *Science.* 251:802-4 (1991)). The mature form of the receptor (HGFR) consists of an extracellular α-subunit and a transmembrane β-subunit containing intrinsic tyrosine kinase activity. Engagement of the receptor induces dimerization which in turn up-regulates kinase activity. Activation of *Met* promotes transphosphorylation of several key tyrosine residues responsible for initiating downstream signaling cascades by recruiting multiple effectors (Furge et al., *Oncogene* 19:5582-9 (2000)). These include the p85 subunit of PI3-kinase, phospholipase Cγ (Gaul et al., *Oncogene* 19:1509-18 (2000)), Grb2 and Shc adaptor proteins, the protein phosphatase SHP2 and Gab1. The latter adapter has emerged as the major downstream docking molecule that becomes tyrosine phosphorylated in response to ligand occupancy (Schaeper et al., *J. Cell Biol.* 149:1419-32 (2000); Bardelli, et al., *Oncogene* 18:1139-46 (1999); and Sachs et al., *J. Cell Biol.* 150:1375-84 (2000)). Activation of other signaling molecules has been reported in HGF stimulated cells, most notably, Ras, MAP kinases and FAK (Tanimura et al., *Oncogene* 17:57-65 (1998); and Lai et al., *J. Biol. Chem.* 275:7474-80 (2000)). The role for many of these signaling molecules has been established in cell proliferation but is not as evident in cell dissociation and scattering.

[0005] The hepatocyte growth factor reecptor (HGFR) is expressed predominantly in epithelial cells but has also been detected in endothelial cells, myoblasts, hematopoietic cells and motor neurons. Inappropriate activation of the receptor is implicated in the onset and progression of a number of tumors and in the promotion of metastasis. A direct link between HGFR and cancer has been shown by the identification of missense mutations in the kinase domain which predispose individuals to papillary renal carcinomas (PRC) and hepatocellular carcinomas (HCC) (Giordano et al., *FASEB J* 14:399-406 (2000)).

[0006] Activation of this tyrosine kinase plays a key role in the regulation of migration, invasion and angiogenesis in cancer. The receptor is overexpressed in a significant percentage of human cancers and is amplified during the transition between primary tumors and metastasis. Missense mutations in the tyrosine kinase domain of the gene have been reported in the germline of affected members of PRC and HCC families (Park et al., *Cancer Res.* 59:307-10 (1999); Schmidt et al., *Nature Genetics* 16:68-73 (1997); and Schmidt et al., *Cancer Research* 58:1719-22 (1998)). Most of these genetic lesions represent disease-producing mutations that appear to accelerate carcinogenesis by constitutively activating the receptor. In addition, *in vivo* experiments indicate that autocrine HGF-*Met* signaling plays a significant role in the development and progression of certain malignancies (Bellusci et al., *Oncogene* 9:1091-99 (1994) and Rong et al., *Proc. Natl. Acad. Sci USA* 91:4731-4735 (1994)). It is becoming increasingly evident that the *Met* signaling pathway is involved in the invasive behavior of various tumors by promoting not only tumor spreading, but also neovascularization (Ramirez et al., *Clin. Endocrinol.* 53:635-44 (2000)). Thus, selective, small molecule kinase

modulators are expected to have therapeutic potential for the treatment of cancers in which *Met* receptor activation plays a critical role in the development and progression of primary tumors and secondary metastases. Since HGF is also a known angiogenic, there is the potential for this class of modulators to impact angiogenesis-dependent diseases such as diabetic retinopathy.

[0007] A direct role for HGFR in the metastatic behavior of human malignancy has been documented in the literature since its initial identification as the cellular homologue of the *tpr-Met* oncogene (Cooper et al., *Nature* 311:29-33 (1984)). The receptor is overexpressed in various tumors including thyroid, ovarian and pancreatic carcinomas and is amplified in liver metastases of colorectal carcinomas (Rong et al., *Cancer Res.* 55:1963-1970 (1995); Rong et al., *Cancer Res.* 53:5355-5360 (1993); Kenworthy et al., *Br. J. Cancer* 66:243-247 (1992); and Scarpino et al., *J. Pathology* 189:570-575 (1999)). In patients with invasive breast carcinoma, expression of either the receptor or ligand is a predictor of decreased survival, further linking *Met* to tumor progression (Camp et al., *Cancer* 86:2259-65 (1999)). In general, most human tumors and tumor cell lines of mesenchymal origin inappropriately express HGFR and/or HGF. This observation supports the premise that HGFR plays a key role in sarcomagenesis and that both autocrine and paracrine signaling modes contribute to the development of human tumors of mesenchymal origin.

[0008] HGFR was originally identified as the cellular counterpart of the *tpr-Met* oncogene, the product of a chromosomal rearrangement generating a chimeric gene by fusing a leucine zipper motif to the tyrosine kinase domain of HGFR (Cooper et al., *Nature* 311:29-33 (1984)). The *tpr-Met* oncogene is activated via the leucine zipper interaction that is responsible for deregulating the enzymatic activity of the kinase domain. Accordingly, the *tpr-Met* oncogene efficiently transforms NIH-3T3 fibroblasts and transgenic expression of this oncogene leads to the development of hyperplasia and tumors in mice (Liang et al., *J. Clin. Invest.* 97:2872-2877 (1996)).

[0009] Almost a decade ago, Vande Woude's lab made the observation that mouse NIH 3T3 fibroblasts that overexpress *Met* can induce tumor formation in nude mice via an autocrine mechanism resulting in the interaction between recombinant *Met* receptor and endogenously expressed ligand (Rong et al., *Proc Natl Acad Sci USA* 91:4731-4735 (1994)). They also showed the transformed cells to be metastatic. Since then numerous reports have substantiated the initial observation that chronic *Met*-HGF signaling can induce tumor formation (Oda et al., *Human Pathology* 31: 185-192 (2000)). For example, spontaneously transformed tumor cells, which express both ligand and receptor, routinely exhibit increased proliferation and motility. The co-expression of HGF and HGFR is common among non-small-cell lung cancers, especially adenocarcinoma. Not surprisingly, retroviral transduction of HGF in NCI-H358 lung adenocarcinoma cells that express HGFR endows these cells with enhanced capacity to colonize soft agar medium and to form xenograft tumors when implanted in immune-deficient mice (Seung et al., *Neoplasia* 2:226-234 (2000)).

[0010] The most compelling data linking HGFR signaling to human malignancies is the discovery of germline missense mutations that map to the kinase domain of HGFR in the majority of hereditary papillary renal cell carcinomas and the detection of somatic missense HGFR mutations in sporadic papillary kidney carcinomas and childhood hepatocellular carcinomas. These mutations which render the receptor constitutively active have been shown to confer an invasive phenotype to transfected cells (Jeffers et al., *Proc. Natl. Acad. Sci. USA* 94:11445-11450 (1997)).

[0011] The introduction of these mutations into wild-type *Met* cDNA results in transforming, tumorigenic, and metastatic properties in mouse cell lines. When these same mutations are introduced into mice as transgenes, the founders develop tumors that metastasize to secondary sites. Furthermore, it has been observed that cells carrying these *Met* mutations undergo clonal expansion during HNSCC (head and neck squamous cell carcinoma) progression, further correlating *Met* with the progression of primary cancers to metastasis (Renzo et al., *Oncogene* 19:1547-1555 (2000)).

[0012] Direct experimental evidence linking the *Met*-HGF signaling pathway to tumor cell metastasis has been validated in the mouse, using either transfected cells or transgenic animals (Takayama et al., *Proc. Natl. Acad. Sci. USA* 94: 701-706 (1997)). For example, in rigorously controlled experiments, anti-Met oligonucleotides inhibit the proliferation and invasiveness of human gastric cancer cells (Kaji et al., *Cancer Gene Therapy* 3:393-404 (1996)). Dominant negative *Met* has been shown by numerous laboratories to reduce tumorigenicity and spontaneous metastasis both *in vitro* and *in vivo* (Firon et al., *Oncogene* 19:2386-2397 (2000)). *In vivo* a dramatic reduction in tumor and metastasis formation, accompanied by improved survival, was noted. Furthermore, peptides corresponding to the multifunctional docking site at the carboxy terminal tail of the *Met* receptor, that bind the receptor and inhibit kinase activity, inhibit HGF-mediated invasive growth, as measured by cell migration, invasivness, and branched morphogenesis (Bardelli et al., J. *Biol. Chem.* 274:29274-29281 (1999)).

[0013] Naturally occurring splice variants of HGF have also been identified that behave as competitive antagonists of mature HGF (Date et al., *Oncogene* 17: 3045-3054 (1998)). These variants inhibit autophosphorylation of the receptor and consequently block HGF-induced migration of human umbilical vein endothelial cells in a migration assay and in an endothelial wounding assay (Jiang et al., *Clinical Cancer Research* **5**:3695-3703 (1999)). HGF antagonists have also been reported to inhibit the motility and invasion of colon, gallbladder and cervical carcinoma cells. Most significantly, infusion of these antagonists into nude mice implanted with tumor cells represses the invasion of tumorigenic cells into surrounding tissues (Kuba et al., *Cancer Research* 60: 6737-6743 (2000)). Similarly, a monoclonal antibody highly selective for HGF has also been found to block tumor progression *in vitro* and *in vivo*. Cao et al., *Proc.*

Nat.l Acad. Sci. USA 98:7443-8 (2001).

[0014] Recently, the geldanamycin family of anisamycin antibiotics has been implicated in the down-regulation of the HGFR at nanomolar concentrations. The loss of HGFR expression observed at nanomolar concentrations not only inhibits HGF-induced cell motility and invasion but also reverts the Met-transformed phenotype (Webb et al., *Cancer Research* 60: 342-349 (2000)). This class of compounds are currently in clinical trials (NCI) as potential anti-invasive, anti-metastatic agents.

[0015] PCT International Publication No. WO 01/09159 discloses nucleic acid ligands to HGF and HGFR. These ligands were isolated using SELEX (Systematic Evolution of Ligands Exponential enrichment). U.S. Patent Nos. 5,686,292 and 6,099,841 report HGFR antagonists and agonists, respectively. U.S. Patent No. 6,174,889 discloses bicyclic heteroaromatic compounds as protein tyrosine kinase inhibitors. PCT International Publication Nos. WO 00/43373, WO 98/07695 and WO 99/15550 disclose protein kinase inhibitor compounds.

[0016] Several attempts have been made to elucidate three dimensional structures of proteins to design candidate drugs (See, e.g., Davis et al., *Science* 291:134-137 (2001); Zhu et al., *Structure* 7: 651-661 (1999); and Ymaguchi et al., *Nature* 384: 484-489 (1996)). Further, PCT International Publication No. WO 00/70030 discloses the three-dimensional crystal structure of Lck with its ligand.

SUMMARY OF THE INVENTION

[0017] The generation, kinetic characterization, and structure determination of the kinase domain of the human HGFR protein is disclosed herein. The domain begins between residues 1051 and 1078 and terminates between residues 1341 and 1348 of the full-length protein [SEQ ID NO: 2]. The domain preferably extends from residues 1051-1341, and more preferably from residues 1051-1348. In one embodiment of the present invention, the domain has the sequence selected from the group of SEQ ID NOS: 3 through 5, 9, 13, 15, and 16.

[0018] In one of its aspects, the present invention relates to an isolated polynucleotide that encodes the human hepatocyte growth factor receptor or the human hepatocyte gowth factor receptor kinase domain, or a fragment or variant thereof. In one embodiment, the nucleotide sequence of the polynucleotide corresponds to at least bases 3342 to 4206 of SEQ ID NO: 1. In other embodiments, the nucleotide sequence of the polynucleotide corresponds to the sequence of SEQ ID NOS: 10, 11, 12, or 14.

[0019] In another of its aspects, the present invention relates to a crystal structure containing the human hepatocyte growth factor receptor kinase. In one embodiment, the amino acid sequence of the kinase corresponds to at least amino acids 1051 to 1348 of SEQ ID NO: 2. In other embodiments, the amino acid sequence of the kinase corresponds to the sequence of SEQ ID NOS: 3, 4, 5, 6, 7, 8, 9, 13, 15, or 16.

[0020] In still another of its aspects, the present invention relates to an isolated polypeptide containing the human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain, or a variant thereof. In one embodiment, the human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain contains a deletion that imparts favorable physical characteristics to the resulting polypeptide (e.g., suitability for analysis by nuclear magnetic resonance, suitability for high throughput screening, suitability for biochemical characterizations, suitability for x-ray crystallography, suitability for colorimetry and suitability for other diagnostic methods). In other embodiments, the polypeptide contains amino acids 1051 to 1341 of the sequence as set forth in SEQ ID NO. 2; amino acids 1051 to 1348 of the sequence as set forth in SEQ ID NO. 2; or the amino acid sequence as set forth in SEQ ID NOS. 3, 4, 5, 6, 7, 8, 9, 13, 15, or 16; or a conservatively substituted variant thereof.

[0021] In yet another of its aspects, the present invention relates to an isolated polynucleotide that encodes the catalytically active form of the human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain, or a fragment or variant thereof.

[0022] A further aspect of the present invention relates to an isolated catalytically active polypeptide comprising the human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain, or a variant thereof.

[0023] Another aspect of the present invention relates to an isolated polynucleotide which encodes the catalytic domain of the human hepatocyte growth factor receptor kinase, or a fragment or variant thereof.

[0024] Still another aspect of the present invention relates to an isolated catalytically active polypeptide containing the catalytic domain of the human hepatocyte growth factor receptor kinase or a variant thereof.

[0025] Yet another aspect of the present invention relates to an isolated soluble polypeptide comprising the catalytic domain of the human hepatocyte growth factor receptor kinase or a variant thereof.

[0026] The present invention also relates to an expression vector for producing the human hepatocyte growth factor receptor kinase in a host cell. The vector contains a polynucleotide encoding the human hepatocyte growth factor receptor kinase or a variant thereof; and regulatory sequences that are functional in the host cell and operably linked to the polynucleotide. In one embodiment, the polynucleotide encodes the active human hepatocyte growth factor receptor kinase containing bases 3342 to 4206 of SEQ ID NO: 1. In another embodiment, the vector is selected from

the group consisting of pET28a, pAcSG2, and pFastBac. In a further embodiment, the host cell is *E. coli.*

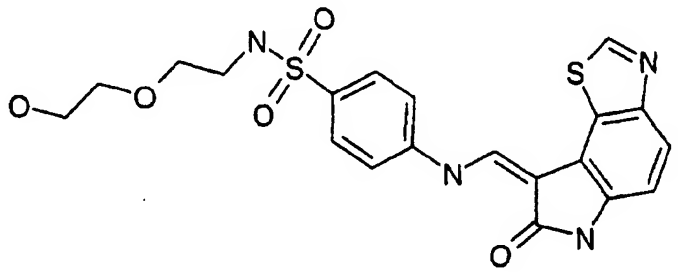
[0027] In another aspect, the present invention relates to a host cell transformed or transfected with a polynucleotide encoding the human hepatocyte growth factor receptor kinase or a variant thereof. In one embodiment, the host cell is transformed or transfected with the polynucleotide via an expression vector containing the polynucleotide; a regulatory sequence functional in the host cell operably linked to the polynucleotide; and a selectable marker. The expression vector can be, for example, pET28a, pAcSG2, and pFastBac. In another embodiment, the polynucleotide encodes the human hepatocyte growth factor receptor kinase containing bases 3342 to 4206 of SEQ ID NO: 1. In a further embodiment, the host cell is *E. coli.* In yet another embodiment, the host cell is infected with a recombinant baculovirus. Additionally, the host cell can be is insect cell, such as Sf9.

[0028] The present invention additionally relates to a method of producing a polypeptide or variant thereof by culturing a host cell, transformed or transfected with a polynucleotide encoding the human hepatocyte growth factor receptor kinase or a variant thereof, under conditions such that the polypeptide or variant thereof is expressed; and recovering the polypeptide or variant.

[0029] In yet another of its aspects, the present invention relates to a method for assaying a candidate compound for its ability to interact with the human hepatocyte growth factor receptor. The method involves expressing an isolated DNA sequence or variant thereof encoding the kinase domain of the human hepatocyte growth factor receptor in a host capable of producing the kinase in a form which may be assayed for interaction with the candidate compound. The kinase is exposed to the candidate compound and the interaction of the kinase with the candidate compound is evaluated. In one embodiment, the interaction is evaluated by crystallizing the kinase in a condition suitable for x-ray crystallography; and conducting x-ray crystallography on the kinase. The results of the x-ray crystallography are optionally used to determine the three dimensional molecular structure of the configuration of human hepatocyte growth factor receptor kinase and the binding pockets thereof.

[0030] The present invention further relates to a crystal structure containing a polypeptide encoded by a polynucleotide which encodes the human hepatocyte growth factor receptor kinase domain, or a fragment or variant thereof.

[0031] In addition, the present invention relates to a crystal structure containing a polypeptide encoded by a polynucleotide which encodes the human hepatocyte growth factor receptor kinase domain, or a fragment or variant thereof, and a ligand complexed thereto. In one embodiment, the ligand modulates the activity of human hepatocyte growth factor kinase. In another embodiment, the ligand is a compound of the formula:



[0032] The present invention still further relates to a process of drug design for compounds which interact with the human hepatocyte growth factor receptor kinase. The process involves crystallizing the human hepatocyte growth factor receptor kinase and resolving the x-ray crystallography of the kinase. The data generated from resolving the x-ray crystallography of the kinase is then applied to a computer algorithm which generates a model of the kinase suitable for use in designing molecules that will act as agonists or antagonists to the polypeptide. An interative process is then applied whereby various molecular structures are applied to the computer-generated model to identify potential agonists or antagonists of the kinase. In one embodiment, the process is utilized to identify modulators of the active kinase, which serve as lead compounds for the design of potentially therapeutic compounds for the treatment of diseases or disorders associated with the hepatocyte growth factor receptor- hepatocyte growth factor signaling pathway.

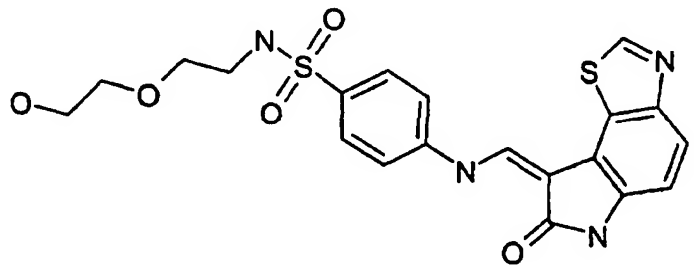
[0033] In yet another aspect, the present invention relates to a method of rapidly screening large compound libraries to identify compounds that inhibit human hepatocyte growth factor receptor kinase containing a non-radioactive immunosorbent assay capable of robotic control. In one embodiment, the assay is DELFIA.

[0034] In still another aspect, the present invention relates to a method of assessing compounds which are agonists or antagonists of the activity of the hepatocyte growth factor receptor kinase by crystallizing the hepatocyte growth factor receptor kinase and obtaining crystallography coordinates for the crystallized hepatocyte growth factor receptor

kinase. The crystallography coordinates are then applied to a computer algorithm such that the algorithm generates a model of the kinase suitable for use in designing molecules that will act as agonists or antagonists to the kinase. An iterative process is used to apply various molecular structures to the computer-generated model to identify potential agonists or antagonists to the kinase. The agonist or antagonist is then optionally synthesized or obtained, and contacted with the molecule to determine the ability of the potential agonist or antagonist to interact with the molecule.

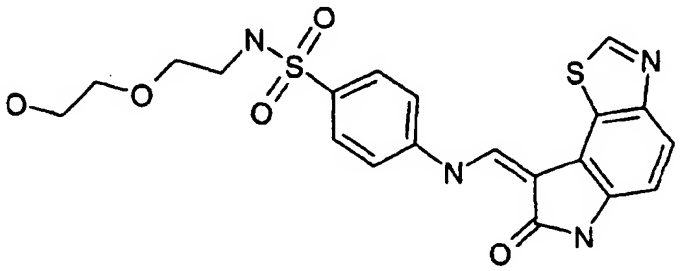
[0035] The present invention also relates to a method for determining the three-dimensional structure of a complex of hepatocyte growth factor receptor kinase with a ligand, wherein x-ray diffraction data for crystals of the complex are obtained, and the set of atomic coordinates of Table 1 or portions thereof; and coordinates having a root mean square deviation therefrom with respect to conserved protein backbone atoms of not more than about 1.5 Å are used to define the three-dimensional structure of the complex.

[0036] In a further of its aspects, the present invention relates to a method of using a three-dimensional structure of a polypeptide encoded by a polynucleotide which encodes the human hepatocyte growth factor receptor and a compound of the formula:



as defined by the structure coordinates of Table 1, or a portion thereof, in a drug-discovery strategy. A potential drug is selected, in conjunction with computer modeling, by performing rational drug design with the three-dimensional structure determined from one or more sets of atomic coordinates in Table 1. The potential drug is contacted with a polypeptide containing a functional human hepatocyte growth factor receptor and the binding of the potential drug with the polypeptide is determined.

[0037] The present invention still further relates to a method of using a three-dimensional structure of a polypeptide encoded by a polynucleotide which encodes the human hepatocyte growth factor receptor kinase domain and a compound of the formula:



as defined by the structure coordinates of Table 1, or a portion thereof, in a drug-discovery strategy. A potential drug is selcted, in conjunction with computer modeling, by performing rational drug design with the three-dimensional structure determined from one or more sets of atomic coordinates in Table 1. The potential drug is contacted with a polypeptide containing a functional human hepatocyte growth factor receptor. Whether or not the potential drug modulates the activity of the polypeptide is then determined.

[0038] The present invention further relates to a method for evaluating the potential of a chemical entity to associate with either: (a) a molecule or molecular complex having a binding pocket defined by structure coordinates of human hepatocyte growth factor receptor amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231, according to Table 1, or (b) a homologue of the molecule or molecular complex having a binding pocket

that has a root mean square deviation from the backbone atoms of the amino acids of not more than about 1.5 Å. The method involves employing computational means to perform a fitting operation between the chemical entity and a binding pocket defined by structure coordinates of hepatocyte growth factor receptor amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231which are within about a root mean square deviation of not more than about 1.5 Å from the backbone atoms of said amino acids according to Table 1; and analyzing the results of the fitting operation to quantify the association between the chemical entity and the binding pocket.

[0039] In yet another of its aspects, the present invention relates to a computer for producing a three-dimensional representation of: (a) a molecule or molecular complex, wherein said molecule or molecular complex comprises a binding pocket defined by the structure coordinates of hepatocyte growth factor receptor kinase amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231, according to Table 1; or (b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than about 1.5 Å. The computer comprises includes a computer-readable data storage medium having a data storage material encoded with computer-readable data containing the structure coordinates of hepatocyte growth factor kinase amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231, according to Table 1. The computer also includes a working memory for storing instructions for processing the computer-readable data; a central-processing unit coupled to the working memory and to the computer-readable data storage medium for processing the computer-machine readable data into the three-dimensional representation; and a display coupled to the central-processing unit for displaying the three-dimensional representation. In one embodiment, the computer produces a three-dimensional representation of: (a) a molecule or molecular complex defined by structure coordinates of all of the hepatocyte growth factor kinase amino acids set forth in Table 1, or (b) a homologue of the molecule or molecular complex having a binding pocket that has a root mean square deviation from the backbone atoms of the amino acids of not more than 1.5 Å.

[0040] The present invention also relates to a computer for determining at least a portion of the structure coordinates corresponding to the x-ray diffraction data obtained from a molecule or molecular complex. The computer includes a computer-readable data storage medium having a data storage material encoded with machine-readable data, wherein the data includes at least a portion of the structural coordinates of hepatocyte growth factor receptor kinase according to Table 1. The computer also includes a computer-readable data storage medium having a data storage material encoded with computer-readable data including x-ray diffraction data obtained from the molecule or molecular complex; a working memory for storing instructions for processing the computer-readable data; a central-processing unit coupled to the working memory and to the computer-readable data storage medium for performing a Fourier transform of the machine readable data and for processing the computer-readable data into structure coordinates; and a display coupled to the central-processing unit for displaying the structure coordinates of the molecule or molecular complex.

[0041] In still another aspect, the present invention relates to a computer readable medium having stored thereon data of the structure coordinates of a *Met* ligand-binding site including 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231 according to Table 1.

BRIEF DESCRIPTION OF THE DRAWINGS

[0042] The numerous objects and advantages of the present invention may be better understood by those skilled in the art by reference to the accompanying detailed description and the following drawings. The application file contains at least one drawing executed in color. Copies of this patent application publication with color drawings will be provided by the Office upon request and payment of the necessary fee.

Figure 1 is a purification scheme of the human HGFRkd;

Figure 2 is a ribbon representation of the kinase domain of the HGFR protein structure with Compound **1** bound thereto, wherein the N- and C-termini are indicated by N and C, respectively. Colors: Compound **1** (purple), Glycine-rich loop (orange), activation loop (yellow), alpha helix C (green), kinase insert domain (red), and remainder of protein (blue);

Figure 3 is a ribbon representation of the kinase domain of the HGFR kinase activation loop. Colors: activation loop (purple), Glycine-rich loop (yellow), alpha helix C (red), Phenylalanine 1089 (light blue), Aspartic acid 1228 (green), and Tyrosine-1230 (dark blue);

Figure 4 is an atomic representation of the Compound **1**-HGFR kinase domain binding area, wherein the positions of bound water molecules are shown as red crosshairs. Colors: carbon (green), nitrogen (blue), oxygen (red), and sulfur (yellow);

Figure 5(A) is a Coomassie stained isoelectric focussing (IEF) electrophoretic evaluation of a time-course (20 °C) of HGFR autophosphorylation;

Figure 5(B) is an autoradiogram of IEF gel;

Figure 5(C) is a kinetic evaluation of the activation time course at 4°C;

Figure 5(D) is a MALDI-TOF evaluation of HGFR and pHGFR peptides derived from an exhaustive tryptic digest;

Figure 5(E) is a parent ion scan by nano-ESI-MS trypsin proteolyzed HGFR;

Figure 6(A) is a graph showing inhibition of HGFR and pHGFR by Compound **1** as measured in the coupled enzymatic assay; and

Figure 6(B) is a graph showing double reciprocal analysis of Compound **1** inhibition of pHGFR.

DETAILED DESCRIPTION OF THE INVENTION AND PREFERRED EMBODIMENTS

[0043] The terms "comprising" and "including" are used herein in their open, non-limiting sense.

[0044] The catalytic domain of the human HGFR receptor kinase facilitated crystallography, enzyme characterization, and high throughput screening of inhibitors. In particular, the catalytic domain of the HGFR kinase domain was used to determine its three-dimensional structure, which provides unique structural information useful for drug design.

[0045] As used herein, the abbreviation 'HGFR' or *'Met'* refers to the polynucleotide encoding the hepatocyte growth factor receptor tyrosine kinase, or the protein *per se.* Also, the abbreviation 'hHGFR' or 'human *Met',* as used herein, refers to the polynucleotide encoding the human hepatocyte growth factor receptor tyrosine kinase or the protein *per se.* The HGFR protein is sometimes referred to as HGFR tyrosine kinase or HGFR kinase throughout the application. The nucleic acid sequence of the polynucleotide encoding the full-length protein of hHGFR was published by Park et al. (*Proc. Natl. Acad. Sci.USA* 84: 6379-83 (1987)) and submitted to GenBank under the accession number NM_000245. The nucleic acid sequence described therein is provided herein, as SEQ ID NO: 1. The corresponding peptide sequence of the full-length protein is provided herein, as SEQ ID NO: 2. This peptide sequence was submitted to GenBank by Park et al. and assigned Accession number P08581. The intracellular domain of HGFR is provided herein as SEQ ID NO. 12.

SEQ ID NO. 1:

cgccctcgcc gcccgcggcg ccccgagcgc tttgtgagca gatgcggagc cgagtggagg
gcgcgagcca gatgcggggc gacagctgac ttgctgagag gaggcgggga ggcgcggagc
gcgcgtgtgg tccttgcgcc gctgacttct ccactggttc ctgggcaccg aaagataaac
ctctcataat gaaggccccc gctgtgcttg cacctggcat cctcgtgctc ctgtttacct
tggtgcagag gagcaatggg gagtgtaaag aggcactagc aaagtccgag atgaatgtga
atatgaagta tcagcttccc aacttcaccg cggaaacacc catccagaat gtcattctac
atgagcatca cattttcctt ggtgccacta actacattta tgttttaaat gaggaagacc
ttcagaaggt tgctgagtac aagactgggc ctgtgctgga acacccagat tgtttcccat
gtcaggactg cagcagcaaa gccaatttat caggaggtgt ttggaaagat aacatcaaca
tggctctagt tgtcgacacc tactatgatg atcaactcat tagctgtggc agcgtcaaca
gagggacctg ccagcgacat gtctttcccc acaatcatac tgctgacata cagtcggagg
ttcactgcat attctcccca cagatagaag agcccagcca gtgtcctgac tgtgtggtga
gcgccctggg agccaaagtc ctttcatctg taaaggaccg gttcatcaac ttctttgtag
gcaataccat aaattcttct tatttcccag atcatccatt gcattcgata tcagtgagaa
ggctaaagga aacgaaagat ggttttatgt ttttgacgga ccagtcctac attgatgttt
tacctgagtt cagagattct taccccatta agtatgtcca tgcctttgaa agcaacaatt

ttatttactt cttgacggtc caaagggaaa ctctagatgc tcagactttt cacacaagaa
taatcaggtt ctgttccata aactctggat tgcattccta catggaaatg cctctggagt
gtattctcac agaaaagaga aaaaagagat ccacaaagaa ggaagtgttt aatatacttc
aggctgcgta tgtcagcaag cctggggccc agcttgctag acaaatagga gccagcctga
atgatgacat tcttttcggg gtgttcgcac aaagcaagcc agattctgcc gaaccaatgg
atcgatctgc catgtgtgca ttccctatca aatatgtcaa cgacttcttc aacaagatcg
tcaacaaaaa caatgtgaga tgtctccagc atttttacgg acccaatcat gagcactgct
ttaataggac acttctgaga aattcatcag gctgtgaagc gcgccgtgat gaatatcgaa
cagagtttac cacagctttg cagcgcgttg acttattcat gggtcaattc agcgaagtcc
tcttaacatc tatatccacc ttcattaaag gagacctcac catagctaat cttgggacat
cagagggtcg cttcatgcag gttgtggttt ctcgatcagg accatcaacc cctcatgtga
attttctcct ggactcccat ccagtgtctc cagaagtgat tgtggagcat acattaaacc
aaaatggcta cacactggtt atcactggga agaagatcac gaagatccca ttgaatggct
tgggctgcag acatttccag tcctgcagtc aatgcctctc tgccccaccc tttgttcagt
gtggctggtg ccacgacaaa tgtgtgcgat cggaggaatg cctgagcggg acatggactc
aacagatctg tctgcctgca atctacaagg ttttcccaaa tagtgcaccc cttgaaggag
ggacaaggct gaccatatgt ggctgggact ttggatttcg gaggaataat aaatttgatt
taaagaaaac tagagttctc cttggaaatg agagctgcac cttgacttta agtgagagca
cgatgaatac attgaaatgc acagttggtc ctgccatgaa taagcatttc aatatgtcca
taattatttc aaatggccac gggacaacac aatacagtac attctcctat gtggatcctg
taataacaag tatttcgccg aaatacggtc ctatggctgg tggcacttta cttactttaa
ctggaaatta cctaaacagt gggaattcta gacacatttc aattggtgga aaaacatgta
ctttaaaaag tgtgtcaaac agtattcttg aatgttatac cccagcccaa accatttcaa
ctgagtttgc tgttaaattg aaaattgact tagccaaccg agagacaagc atcttcagtt
accgtgaaga tcccattgtc tatgaaattc atccaaccaa atcttttatt agtacttggt
ggaaagaacc tctcaacatt gtcagttttc tattttgctt tgccagtggt gggagcacaa
taacaggtgt tgggaaaaac ctgaattcag ttagtgtccc gagaatggtc ataaatgtgc
atgaagcagg aaggaacttt acagtggcat gtcaacatcg ctctaattca gagataatct
gttgtaccac tccttccctg caacagctga atctgcaact ccccctgaaa accaaagcct
ttttcatgtt agatgggatc ctttccaaat actttgatct catttatgta cataatcctg
tgtttaagcc ttttgaaaag ccagtgatga tctcaatggg caatgaaaat gtactggaaa
ttaagggaaa tgatattgac cctgaagcag ttaaaggtga agtgttaaaa gttggaaata
agagctgtga gaatatacac ttacattctg aagccgtttt atgcacggtc cccaatgacc
tgctgaaatt gaacagcgag ctaaatatag agtggaagca agcaatttct tcaaccgtcc
ttggaaaagt aatagttcaa ccagatcaga atttcacagg attgattgct ggtgttgtct
caatatcaac agcactgtta ttactacttg ggtttttcct gtggctgaaa aagagaaagc
aaattaaaga tctgggcagt gaattagttc gctacgatgc aagagtacac actcctcatt
tggataggct tgtaagtgcc cgaagtgtaa gcccaactac agaaatggtt tcaaatgaat
ctgtagacta ccgagctact tttccagaag atcagtttcc taattcatct cagaacggtt
catgccgaca agtgcagtat cctctgacag acatgtcccc catcctaact agtggggact
ctgatatatc cagtccatta ctgcaaaata ctgtccacat tgacctcagt gctctaaatc
cagagctggt ccaggcagtg cagcatgtag tgattgggcc cagtagcctg attgtgcatt
tcaatgaagt cataggaaga gggcatttg gttgtgtata tcatgggact ttgttggaca
atgatggcaa gaaaattcac tgtgctgtga aatccttgaa cagaatcact gacataggag
aagtttccca atttctgacc gagggaatca tcatgaaaga ttttagtcat cccaatgtcc

tctcgctcct gggaatctgc ctgcgaagtg aagggtctcc gctggtggtc ctaccataca
tgaaacatgg agatcttcga aatttcattc gaaatgagac tcataatcca actgtaaaag
atcttattgg ctttggtctt caagtagcca aagcgatgaa atatcttgca agcaaaaagt
ttgtccacag agacttggct gcaagaaact gtatgctgga tgaaaaattc acagtcaagg
ttgctgattt tggtcttgcc agagacatgt atgataaaga atactatagt gtacacaaca
aaacaggtgc aaagctgcca gtgaagtgga tggctttgga aagtctgcaa actcaaaagt
ttaccaccaa gtcagatgtg tggtcctttg gcgtcgtcct ctgggagctg atgacaagag
gagccccacc ttatcctgac gtaaacacct ttgatataac tgtttacttg ttgcaaggga
gaagactcct acaacccgaa tactgcccag acccccttata tgaagtaatg ctaaaatgct
ggcaccctaa agccgaaatg cgcccatcct tttctgaact ggtgtcccgg atatcagcga
tcttctctac tttcattggg gagcactatg tccatgtgaa cgctacttat gtgaacgtaa
aatgtgtcgc tccgtatcct tctctgttgt catcagaaga taacgctgat gatgaggtgg
acacacgacc agcctccttc tgggagacat catagtgcta gtactatgtc aaagcaacag
tccacacttt gtccaatggt tttttcactg cctgaccttt aaaaggccat cgatattctt
tgctccttgc cataggactt gtattgttat ttaaattact ggattctaag gaatttctta
tctgacagag catcagaacc agaggcttgg tcccacaggc cagggaccaa tgcgctgcag

SEQ ID NO. 2:

MKAPAVLAPGILVLLFTLVQRSNGECKEALAKSEMNVNMKYQLPNFTAETPIQNVIL
HEHHIFLGATNYIYVLNEEDLQKVAEYKTGPVLEHPDCFPCQDCSSKANLSGGVWKD
NINMALVVDTYYDDQLISCGSVNRGTCQRHVFPHNHTADIQSEVHCIFSPQIEEPSQCP
DCVVSALGAKVLSSVKDRFINFFVGNTINSSYFPDHPLHSISVRRLKETKDGFMFLTD
QSYIDVLPEFRDSYPIKYVHAFESNNFIYFLTVQRETLDAQTFHTRIIRFCSINSGLHSY
MEMPLECILTEKRKKRSTKKEVFNILQAAYVSKPGAQLARQIGASLNDDILFGVFAQS
KPDSAEPMDRSAMCAFPIKYVNDFFNKIVNKNNVRCLQHFYGPNHEHCFNRTLLRNS
SGCEARRDEYRTEFTTALQRVDLFMGQFSEVLLTSISTFIKGDLTIANLGTSEGRFMQV
VVSRSGPSTPHVNFLLDSHPVSPEVIVEHTLNQNGYTLVITGKKITKIPLNGLGCRHFQ
SCSQCLSAPPFVQCGWCHDKCVRSEECLSGTWTQQICLPAIYKVFPNSAPLEGGTRLT
ICGWDFGFRRNNKFDLKKTRVLLGNESCTLTLSESTMNTLKCTVGPAMNKHFNMSIII
SNGHGTTQYSTFSYVDPVITSISPKYGPMAGGTLLTLTGNYLNSGNSRHISIGGKTCTL
KSVSNSILECYTPAQTISTEFAVKLKIDLANRETSIFSYREDPIVYEIHPTKSFISGGSTIT
GVGKNLNSVSVPRMVINVHEAGRNFTVACQHRSNSEIICCTTPSLQQLNLQLPLKTKA
FFMLDGILSKYFDLIYVHNPVFKPFEKPVMISMGNENVLEIKGNDIDPEAVKGEVLKV
GNKSCENIHLHSEAVLCTVPNDLLKLNSELNIEWKQAISSTVLGKVIVQPDQNFTGLIA
GVVSISTALLLLLGFFLWLKKRKQIKDLGSELVRYDARVHTPHLDRLVSARSVSPTTE
MVSNESVDYRATFPEDQFPNSSQNGSCRQVQYPLTDMSPILTSGDSDISSPLLQNTVHI
DLSALNPELVQAVQHVVIGPSSLIVHFNEVIGRGHFGCVYHGTLLDNDGKKIHCAVK
SLNRITDIGEVSQFLTEGIIMKDFSHPNVLSLLGICLRSEGSPLVVLPYMKHGDLRNFIR
NETHNPTVKDLIGFGLQVAKGMKYLASKKFVHRDLAARNCMLDEKFTVKVADFGL
ARDMYDKEYYSVHNKTGAKLPVKWMALESLQTQKFTTKSDVWSFGVVLWELMTR
GAPPYPDVNTFDITVYLLQGRRLLQPEYCPDPLYEVMLKCWHPKAEMRPSFSELVSRI
SAIFSTFIGEHYVHVNATYVNVKCVAPYPSLLSSEDNADDEVDTRPASFWETS

SEQ ID NO. 12:

atgggcagtgaattagttcgctacgatgcaagagtacacactcctcatttggataggcttgtaagtgcccgaagtgtaagcccaactaca
gaaatggtttcaaatgaatctgtagactaccgagctacttttccagaagatcagtttcctaattcatctcagaacggttcatgccgacaagt
gcagtatcctctgacagacatgtccccatcctaactagtggggactctgatatatccagtccattactgcaaaatactgtccacattgacc
tcagtgctctaaatccagagctggtccaggcagtgcagcatgtagtgattgggcccagtagcctgattgtgcatttcaatgaagtcatag
gaagagggcattttggttgtgtatatcatgggactttgttggacaatgatggcaagaaaattcactgtgctgtgaaatccttgaacagaatc
actgacataggagaagtttcccaatttctggccgaggaatcatcatgaaagattttagtcatcccaatgtcctctcgctcctgggaatctg
cctgcgaagtgaagggtctccgctggtggtcctaccatacatgaaacatggagatcttcgaaatttcattcgaaatgagactcataatcca
actgtaaaagatcttattggctttggtcttcaagtagccaaaggcatgaaatatcttgcaagcaaaaagtttgtccacagagacttggctgc
aagaaactgtatgctggatgaaaaattcacagtcaaggttgctgattttggtcttgccagagacatgtatgataaagaatactatagtgtac
acaacaaaacaggtgcaaagctgccagtgaagtggatggctttggaaagtctgcaaactcaaaagtttaccaccaagtcagatgtgtg
gtcctttggcgtgctcctctgggagctgatgacaagaggagccccaccttatcctgatgtaaacacctttgatataactgtttacttgttgca
agggagaagactcctacaacccgaatactgcccagacccccttatatgaagtaatgctaaaatgctggcaccctaaagccgaaatgcgc
ccatccttttctgaactggtgtcccggatatcagcaatcttctctactttcattggggagcactatgtccatgtgaacgctacttatgtgaacg
taaaatgtgtcgctccatatccatctctgttgtcatcagaagataacgctgatgatgaggtggacacacgaccagcctccttctgggagac
atca

[0046] As used herein, the abbreviation 'HGFRkd' refers to the catalytic domain of the hHGFR, said domain beginning between residues 1051 and 1078 and terminating between residues 1341 and 1348 of the full-length protein [SEQ ID NO: 2]. According to certain embodiments of the present invention: (1) a methionine residue is added to the very N-terminal of the HGFRkd sequence [SEQ ID NO: 3]; (2) residues 1051-1349 of the hepatocyte growth factor receptor precursor wherein a methionine residue has been added to the very N-terminus of the sequence, the glycine at residue 1191 has been replaced by alanine, and the valine at position 1272 has been replaced by leucine [SEQ ID NO. 4]; (3) the valine at position 1272 is replaced by leucine [SEQ ID NO. 5]; (4) the methionine at residue 1250 is replaced by threonine [SEQ ID NO. 9; a naturally occurring variant in hepatocellular carcinoma (HPRC)]; (5) the histidine at residue 1094 is replaced by arginine [SEQ ID NO. 15]; and/or (6) the tyrosine at residue 1230 is replaced by cysteine [SEQ ID NO. 16].

SEQ ID NO. 3:

VHIDLSALN PELVQAVQHV VIGPSSLIVH FNEVIGRGHF GCVYHGTLLD
NDGKKIHCAV KSLNRITDIG EVSQFLTEGI IMKDFSHPNV LSLLGICLRS EGSPLVVLPY
MKHGDLRNFI RNETHNPTVK DLIGFGLQVA KGMKYLASKK FVHRDLAARN
CMLDEKFTVK VADFGLARDM YDKEYYSVHN KTGAKLPVKW MALESLQTQK
FTTKSDVWSF GVVLWELMTR GAPPYPDVNT FDITVYLLQG RRLLQPEYCP
DPLYEVMLKC WHPKAEMRPS FSELVSRISA IFSTFIGEH

SEQ ID NO.: 4

MVHIDLSALN PELVQAVQHV VIGPSSLIVH FNEVIGRGHF GCVYHGTLLD
NDGKKIHCAV KSLNRITDIG EVSQFLTEGI IMKDFSHPNV LSLLGICLRS
EGSPLVVLPY MKHGDLRNFI RNETHNPTVK DLIGFGLQVA KAMKYLASKK
FVHRDLAARN CMLDEKFTVK VADFGLARDM YDKEYYSVHN KTGAKLPVKW
MALESLQTQK FTTKSDVWSF GVLLWELMTR GAPPYPDVNT FDITVYLLQG
RRLLQPEYCP DPLYEVMLKC WHPKAEMRPS FSELVSRISA IFSTFIGEH

SEQ ID NO.: 5

MVHIDLSALN PELVQAVQHV VIGPSSLIVH FNEVIGRGHF GCVYHGTLLD
NDGKKIHCAV KSLNRITDIG EVSQFLTEGI IMKDFSHPNV LSLLGICLRS
EGSPLVVLPY MKHGDLRNFI RNETHNPTVK DLIGFGLQVA KGMKYLASKK
FVHRDLAARN CMLDEKFTVK VADFGLARDM YDKEYYSVHN KTGAKLPVKW
MALESLQTQK FTTKSDVWSF GVLLWELMTR GAPPYPDVNT FDITVYLLQG
RRLLQPEYCP DPLYEVMLKC WHPKAEMRPS FSELVSRISA IFSTFIGEH

SEQ ID NO.: 9

MVHIDLSALN PELVQAVQHV VIGPSSLIVH FNEVIGRGHF GCVYHGTLLD
NDGKKIHCAV KSLNRITDIG EVSQFLTEGI IMKDFSHPNV LSLLGICLRS
EGSPLVVLPY MKHGDLRNFI RNETHNPTVK DLIGFGLQVA KAMKYLASKK
FVHRDLAARN CMLDEKFTVK VADFGLARDM YDKEYYSVHN KTGAKLPVKW
TALESLQTQK FTTKSDVWSF GVLLWELMTR GAPPYPDVNT FDITVYLLQG
RRLLQPEYCP DPLYEVMLKC WHPKAEMRPS FSELVSRISA IFSTFIGEH

SEQ ID NO.: 15:

MVHIDLSALN PELVQAVQHV VIGPSSLIVH FNEVIGRGHF GCVYRGTLLD
NDGKKIHCAV KSLNRITDIG EVSQFLTEGI IMKDFSHPNV LSLLGICLRS
EGSPLVVLPY MKHGDLRNFI RNETHNPTVK DLIGFGLQVA KAMKYLASKK
FVHRDLAARN CMLDEKFTVK VADFGLARDM YDKEYYSVHN KTGAKLPVKW
MALESLQTQK FTTKSDVWSF GVLLWELMTR GAPPYPDVNT FDITVYLLQG
RRLLQPEYCP DPLYEVMLKC WHPKAEMRPS FSELVSRISA IFSTFIGEH

SEQ ID NO.: 16

MVHIDLSALN PELVQAVQHV VIGPSSLIVH FNEVIGRGHF GCVYHGTLLD
NDGKKIHCAV KSLNRITDIG EVSQFLTEGI IMKDFSHPNV LSLLGICLRS
EGSPLVVLPY MKHGDLRNFI RNETHNPTVK DLIGFGLQVA KAMKYLASKK
FVHRDLAARN CMLDEKFTVK VADFGLARDM CDKEYYSVHN KTGAKLPVKW
MALESLQTQK FTTKSDVWSF GVLLWELMTR GAPPYPDVNT FDITVYLLQG
RRLLQPEYCP DPLYEVMLKC WHPKAEMRPS FSELVSRISA IFSTFIGEH

[0047] As used herein, the abbreviation 'pHGFR' refers to phosphorylated HGFR.

A. Peptides, Proteins and Antibodies

[0048] The present invention provides isolated peptide and protein molecules that are comprised of, consist of, or consist essentially of the amino acid sequences of the kinase peptides encoded by the nucleic acid sequence disclosed in the SEQ ID NO: 1, as well as all obvious variants of these peptides that are within the art to make and use. Some of these variants are described in detail below.

[0049] As used herein, the terms "kinase", "kinase peptide" and "protein kinase" refer to enzymes that catalyze the transfer of a phosphate residue from a nucleoside triphosphate to an amino acid side chain in selected targets. The covalent phosphorylation in turn regulates the activity of the target protein. In addition, phosphorylation frequently acts as the signal that triggers a particular process or reaction, playing an integral part in cellular regulation and control mechanisms. Inappropriate or unregulated phosphorylation can result in errors in cell signaling and the associated cell cycle and regulation processes. Most protein kinases are highly substrate specific. Those that have the ability to phos-

phorylate numerous substrates frequently turn out to be oncogenes, genes that are associated with neoplastic transformation of a cell.

[0050] As used herein, the term "catalytically active form" refers to any form of peptides or proteins exhibiting intrinsic enzymatic activity. Preferably, the term "catalytically active form" refers to peptides or proteins capable of autophosphorylation.

[0051] As used herein, a peptide is said to be "isolated" or "purified" when it is free or substantially free of cellular material and/or free or substantially free of chemical precursors or other chemicals. The peptides of the present invention can be purified to homogeneity or other degrees of purity. The level of purification will be based primarily on the intended use. The critical feature is that the preparation allows for the desired function of the peptide, even if in the presence of considerable amounts of other components.

[0052] In some uses, "substantially free of cellular material" includes preparations of the peptide having less than about 30% (by dry weight) other proteins (i.e., contaminating protein), preferably less than about 20% other proteins, more preferably less than about 10% other proteins, or even more preferably less than about 5% other proteins. When the peptide is recombinantly produced, it can also be substantially free of culture medium, i.e., culture medium represents less than about 20% of the volume of the protein preparation.

[0053] The language "substantially free of chemical precursors or other chemicals" includes preparations of the peptide in which it is separated from chemical precursors or other chemicals that are involved in its synthesis. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of the kinase peptide having less than about 30% (by dry weight) chemical precursors or other chemicals, preferably less than about 20% chemical precursors or other chemicals, more preferably less than about 10% chemical precursors or other chemicals, or even more preferably less than about 5% chemical precursors or other chemicals.

[0054] The isolated kinase described herein can be purified from cells that naturally express it, purified from cells that have been altered to express it (recombination), or synthesized using known protein synthesis methods. For example, a nucleic acid molecule encoding the protein kinase is cloned into an expression vector, the expression vector introduced into a host cell and the protein expressed in the host cell. The protein can then be isolated from the cells by an appropriate purification scheme using standard protein purification techniques. Many of these techniques are described in detail below.

[0055] As mentioned above, the present invention also provides variants of the amino acid sequence of the peptides of the present invention, such as naturally occurring mature forms of the peptides, allelic/sequence variants of the peptides, non-naturally occurring recombinantly derived variants of the peptides, and orthologs and paralogs of the peptides. Such variants can be generated using techniques that are known by those skilled in the fields of recombinant nucleic acid technology and protein biochemistry. In addition, such variants can readily be identified/made using molecular techniques and the sequence information disclosed herein. Further, such variants can readily be distinguished from other peptides based on sequence and/or structural homology to the peptides of the present invention. The degree of homology/identity present will be based primarily on whether the peptide is a functional variant or non-functional variant, the amount of divergence present in the paralog family and the evolutionary distance between the orthologs.

[0056] To determine the percent identity of two amino acid sequences or two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid 'identity' is equivalent to amino acid or nucleic acid 'homology'). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences. In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least about 40%, preferably about 50%, more preferably about 60%, even more preferably about 70%, still more preferably about 80%, and yet more preferably about 90% or more of the length of the reference sequence.

[0057] The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. See, e.g., *Computational Molecular Biology,* Lesk, A.M., ed., Oxford University Press, New York (1988); *Biocomputing: Informatics and Genome Projects,* Smith, D.W., ed., Academic Press, New York (1993); *Computer Analysis of Sequence Data, Part 1,* Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey (1994); *Sequence Analysis in Molecular Biology,* von Heinje, G., Academic Press (1987); and *Sequence Analysis Primer,* Gribskov, M. and Devereux, J., eds., M Stockton Press, New York (1991). In one embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into commercially available computer programs, such as GAP in the GCG software package, using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity

between two nucleotide sequences is determined using the commercially available computer programs including the GAP program in the GCG software package (Devereux, J., et al., *Nucleic Acids Res.* 12(1):387 (1984)), the NWS gap DNA CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into commercially available computer programs, such as ALIGN (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

[0058] The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against sequence databases to, for example, identify other family members or related sequences. Such searches can be performed using commercially available search engines, such as the NBLAST and XBLAST programs (version 2.0) of Altschul et al., *J. Mol. Biol.* 215:403-10 (1990). BLAST nucleotide searches can be performed, for example, with the NBLAST program, score = 100, wordlength = 12, to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches can be performed, for example, with the XBLAST program, score = 50, wordlength = 3, to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. *(Nucleic Acids Res.* 25(17):3389-3402 (1997)). When utilizing BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See, e.g., http://www.ncbi.nlm.nih.gov.

[0059] As used herein, two proteins (or a region of the proteins) have significant homology when the amino acid sequences are preferably at least about 70-75%, more preferably at least about 80-85%, and even more preferably at least about 90-95% or more homologous. A significantly homologous amino acid sequence, according to the present invention, will be encoded by a nucleic acid sequence that will hybridize to a peptide encoding nucleic acid molecule under stringent conditions as more fully described below. Peptides can readily be identified as having a high degree of (i.e., significant) sequence homology/identity to the peptides of the present invention. Full-length clones comprising one of the peptides of the present invention can readily be identified as having complete sequence identity to one of the kinases of the present invention as well as being encoded by the same genetic locus as the kinase provided herein. Allelic variants of a peptide can readily be identified as having a high degree of sequence homology/identity to at least a portion of the peptide as well as being encoded by the same genetic locus as the kinase peptide provided herein.

[0060] Paralogs of a hepatocyte growth factor receptor kinase can readily be identified as having some degree of significant sequence homology/identity to at least a portion of the HGFR, as being encoded by a gene from humans, and as having similar activity or function. Two proteins will typically be considered paralogs when the amino acid sequences are preferably at least about 60% or greater, and more preferably at least about 70% or greater homology through a given region or domain. Such paralogs will be encoded by a nucleic acid sequence that will hybridize to a HGFR encoding nucleic acid molecule under moderate to stringent conditions as more fully described below.

[0061] Orthologs of a kinase peptide can readily be identified as having some degree of significant sequence homology/identity to at least a portion of the kinase peptide as well as being encoded by a gene from another organism. Preferred orthologs will be isolated from mammals. Such orthologs will be encoded by a nucleic acid sequence that will hybridize to a kinase peptide encoding nucleic acid molecule under moderate to stringent conditions, as more fully described below, depending on the degree of relatedness of the two organisms yielding the proteins.

[0062] Non-naturally occurring variants of the kinases of the present invention can readily be generated using recombinant techniques. Such variants include, but are not limited to deletions, additions and substitutions in the amino acid sequence of the kinase. For example, one class of substitutions are conserved amino acid substitutions. Such substitutions are those that substitute a given amino acid in a kinase peptide by another amino acid of like characteristics. Typically seen as conservative substitutions are the replacements, one for another, among the aliphatic amino acids Ala, Val, Leu, and Ile; interchange of the hydroxyl residues Ser and Thr; exchange of the acidic residues Asp and Glu; substitution between the amide residues Asn and Gln; exchange of the basic residues Lys and Arg; and replacements among the aromatic residues Phe and Tyr. Guidance concerning which amino acid changes are likely to be phenotypically silent are found in Bowie et al., *Science 247*:1306-1310 (1990).

[0063] Variant kinases can be fully functional or may have reduced or decreased activity when compared to the wild-type protein. Fully functional variants may contain only conservative variations or variations in non-critical residues or in non-critical regions. Functional variants can also contain substitutions of similar amino acids, which result in no change or an insignificant change in function. Alternatively, such substitutions may positively or negatively affect function to some degree. Non-functional variants typically contain one or more non-conservative amino acid substitutions, deletions, insertions, inversions, or truncations or a substitution, insertion, inversion, or deletion in a critical residue or critical region.

[0064] Amino acids that are essential for function can be identified by methods known in the art, such as site-directed mutagenesis or alanine-scanning mutagenesis (Cunningham et al., *Science* 244:1081-1085 (1989)). The latter procedure introduces single alanine mutations at every residue in the molecule. The resulting mutant molecules are then tested for biological activity, for example by measuring enzymatic activity. Sites that are critical for binding can also be

determined by structural analysis such as X-ray crystallography, nuclear magnetic resonance or photoaffinity labeling (Smith et al., *J. Mol. Biol.* 224:899-904 (1992); de Vos et al., *Science* 255:306-312 (1992)). Accordingly, the peptides of the present invention also encompass derivatives or analogs in which a substituted amino acid residue is not one encoded by the genetic code; in which a substituent group is included; in which the polypeptide is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol); or in which the additional amino acids are fused to the polypeptide, such as a leader or secretory sequence or a sequence for purification of the mature polypeptide or a pro-protein sequence.

[0065] The present invention further provides for functional, active fragments of the kinase peptides, in addition to proteins and peptides that comprise and consist of such fragments. As used herein, a fragment comprises at least about 8 or more contiguous amino acid residues from the protein kinase. Such fragments can be chosen based on the ability to retain one or more of the biological activities of the kinase or could be chosen for the ability to perform a function, e.g. act as an immunogen. Preferred are fragments that are catalytically active and that have improved crystallographic properties as compared to the full-length, wild-type kinase. Such fragments will typically comprise a domain or motif of the kinase, e.g., active site. Further, possible fragments include, but are not limited to, domain or motif containing fragments, soluble peptide fragments, and fragments containing immunogenic structures. Predicted domains and functional sites are readily identifiable by computer programs known and readily available to those of skill in the art (e.g., by PROSITE analysis- Hofmann et al., *Nucleic Acids Res.* 27:215-219 (1999); Bucher et al., *Proceedings 2nd International Conference on Intelligent Systems for Molecular Biology* AAAI Press, Menlo Park, 53-61 (1994)). For example, the fragment can comprise the HGFR intracellular domain [SEQ ID NO. 13].

SEQ ID NO. 13:

MGSELVRYDARVHTPHLDRLVSARSVSPTTEMVSNESVDYRATFPEDQFPNSSQNGS
CRQVQYPLTDMSPILTSGDSDISSPLLQNTVHIDLSALNPELVQAVQHVVIGPSSLIVHF
NEVIGRGHFGCVYHGTLLDNDGKKIHCAVKSLNRITDIGEVSQFLAEGIIMKDFSHPN
VLSLLGICLRSEGSPLVVLPYMKHGDLRNFIRNETHNPTVKDLIGFGLQVAKGMKYL

ASKKFVHRDLAARNCMLDEKFTVKVADFGLARDMYDKEYYSVHNKTGAKLPVKW
MALESLQTQKFTTKSDVWSFGVLLWELMTRGAPPYPDVNTFDITVYLLQGRRLLQPE
YCPDPLYEVMLKCWHPKAEMRPSFSELVSRISAIFSTFIGEHYVHVNATYVNVKCVA
PYPSLLSSEDNADDEVDTRPASFWETS

[0066] A fragment is a variant peptide having an amino acid sequence that is entirely the same as part, but not all, of any amino acid sequence of any peptide of the invention. Fragments may be free standing or comprised within a larger peptide.

[0067] Polypeptides of the present invention also optionally contain amino acids other than the 20 amino acids commonly referred to as the 20 naturally-occurring amino acids. Further, amino acids, including the terminal amino acids, may be modified by natural processes, such as processing and other post-translational modifications, or by chemical modification techniques known in the art. Common modifications that occur naturally in polypeptides are described in basic texts, detailed monographs, and the research literature. Known modifications include, but are not limited to, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent crosslinks, formation of cystine, formation of pyroglutamate, formylation, gamma carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, phenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. Several particularly common modifications, glycosylation, lipid attachment, sulfation, gamma-carboxylation of glutamic acid residues, hydroxylation and ADP-ribosylation, for instance, are described in most basic texts, such as *Proteins - Structure and Molecular Properties,* 2nd Ed., T.E. Creighton, W. H. Freeman and Company, New York (1993). Many detailed reviews are available on this subject, such as by Wold, F., *Posttranslational Covalent Modification of Proteins,* B.C. Johnson, Ed., Academic Press, New York 1-12 (1983); Seifter et al., *Meth. Enzymol. 182:* 626-646 (1990) and Rattan et al., *Ann. N.Y. Acad. Sci. 663*:48-62 (1992).

[0068] As used herein, "polypeptide" refers to any peptide or protein comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres. "Polypeptide" refers to both short chains, commonly referred to as peptides, oligopeptides or oligomers, and to longer chains, generally referred to as proteins. The terms "peptide," "polypeptide," and "protein" are used interchangeably herein.

[0069] The peptides of the present invention can be attached to heterologous sequences to form chimeric or fusion proteins. Such chimeric and fusion proteins comprise a peptide operatively linked to a heterologous protein. "Operatively linked" indicates that the peptide and the heterologous protein are fused in-frame. The heterologous protein can be fused to the N-terminus or C-terminus of the kinase peptide. The two peptides linked in a fusion peptide are typically derived from two independent sources. Therefore, a fusion peptide comprises two linked peptides not normally found linked in nature. The two peptides may be from the same or different genome. In some uses, the fusion protein does not affect the activity of the peptide *per se*. For example, the fusion protein can include, but is not limited to, enzymatic fusion proteins, for example beta-galactosidase fusions, yeast two-hybrid GAL fusions, poly-His fusions (i.e., HI-tagged), MYC-tagged, and Ig fusions. Such fusion proteins, particularly poly-His fusions, can facilitate the purification of recombinant kinase peptides. In certain host cells (e.g., mammalian host cells), expression and/or secretion of a protein can be increased by using a heterologous signal sequence.

[0070] A chimeric or fusion protein can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different protein sequences are ligated together in-frame in accordance with conventional techniques. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments, which can subsequently be annealed and re-amplified to generate a chimeric gene sequence (see, Ausubel et al., *Current Protocols in Molecular Biology,* (1992)). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST protein, His-tag, or green fluorescent protein). A kinase peptide-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the kinase peptide.

[0071] Herein, the term "antibody" refers to a polypeptide or group of polypeptides which are comprised of at least one antibody combining site or binding domain, said binding domain or combining site formed from the folding of variable domains of an antibody molecule to form three dimensional binding spaces with an internal surface shape and charge distribution complementary to the features of an antigen epitope. The term encompasses immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, such as molecules that contain an antibody combining site or paratope. Exemplary antibody molecules are intact immunoglobulin molecules, substantially intact immunoglobulin molecules and portions of an immunoglobulin molecule, including those known in the art as Fab, FabB, $F(abB)_2$ and F(v).

B. Nucleic Acids and Polynucleotides

[0072] The present invention provides isolated nucleic acid molecules that encode the functional or active kinases of the present invention. Such nucleic acid molecules will consist of, consist essentially of, or comprise a nucleotide sequence that encodes one of the kinase peptides of the present invention, an allelic variant thereof, or an ortholog or paralog thereof.

[0073] The terms "nucleic acid molecule" and "polynucleotide" are used interchangeable in this application. These terms generally refer to any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. These terms are intended to include DNA molecules (e.g., cDNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. These terms include, without limitation, single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions or single-, double- and triple-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded, or triple-stranded regions, or a mixture of single- and double-stranded regions. In addition, "polynucleotide" and "nucleic acid molecule" as used herein refer to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The strands in such regions may be from the same molecule or from different molecules. The regions may include all of one or more of the molecules, but more typically involve only a region of some of the molecules. One of the molecules of a triple-helical region often is an oligonucleotide. As used herein, the terms "polynucleotide(s)" and "nucleic acid molecule" also include DNAs or RNAs as described above that contain one or more modified bases. Thus, DNAs or RNAs with backbones modified for stability or for other reasons are "polynucleotide(s)" as that term is intended herein. Moreover, DNAs or RNAs comprising unusual bases, such as inosine, or modified bases, such as tritylated bases, to name just two examples, are polynucleotides as the term is used herein. It will be appreciated that a great variety of modifications have been made to DNA and RNA that serve many useful purposes known to those of skill in the art. The terms "polynucleotide(s)" and "nucleic acid molecules" as employed herein embraces such chemically, enzymatically or metabolically modified forms of polynucleotides, as well as the chemical forms of DNA and RNA characteristic

of viruses and cells, including, for example, simple and complex cells. "Polynucleotide(s)" also embraces short polynucleotides often referred to as oligonucleotide(s).

[0074] As used herein, an "isolated" nucleic acid molecule is one that is separated from other nucleic acid present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA or cDNA of the organism from which the nucleic acid is derived. However, there can be some flanking nucleotide sequences, for example up to about 5KB, particularly contiguous peptide encoding sequences and peptide encoding sequences within the same gene but separated by introns in the genomic sequence. The important point is that the nucleic acid is isolated from remote and unimportant flanking sequences such that it can be subjected to the specific manipulations described herein, such as recombinant expression, preparation of probes and primers, and other uses specific to the nucleic acid sequences. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, is preferably substantially free of other cellular material, or culture medium when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized. However, the nucleic acid molecule can be fused to other coding or regulatory sequences and still be considered isolated. In some instances, the isolated material will form part of a composition (for example, a crude extract containing other substances), buffer system or reagent mix. In other circumstances, the material may be purified to essential homogeneity, for example as determined by PAGE or column chromatograph such as HPLC.

[0075] For example, recombinant DNA molecules contained in a vector are considered isolated. Further examples of isolated DNA molecules include recombinant DNA molecules maintained in heterologous host cells or purified (partially or substantially) DNA molecules in solution. Isolated RNA molecules include *in vivo* or *in vitro* RNA transcripts of the isolated DNA molecules of the present invention. Isolated nucleic acid molecules according to the present invention further include such molecules produced synthetically.

[0076] The preferred classes of nucleic acid molecules that are comprised of the nucleotide sequences of the present invention are the full-length cDNA molecules and genes and genomic clones since some of the nucleic acid molecules provided herein are fragments of the complete gene that exists in nature. A description of how various types of these nucleic acid molecules can be readily made/isolated is provided herein.

[0077] Full-length genes or portions thereof may be cloned from known sequences using any one of a number of methods known in the art. For example, a method which employs XL-PCR (Perkin-Elmer, Foster City, Calif.) to amplify long pieces of DNA may be used. Other methods for obtaining full-length sequences are known in the art.

[0078] The isolated nucleic acid molecules can encode the active protein plus additional amino or carboxyl-terminal amino acids, or amino acids interior to the mature peptide (when the mature form has more than one peptide chain, for instance). Such sequences may play a role in processing of a protein from precursor to an active form, facilitate protein trafficking, prolong or shorten protein half-life or facilitate manipulation of a protein for assay or production, among other things. As generally is the case *in situ*, the additional amino acids may be processed away from the mature active protein by cellular enzymes.

[0079] Once a full-length gene is cloned, portions of the gene can be obtained using techniques known to those of ordinary skill in the art. The isolated nucleic acid molecules include, but are not limited to, the sequence encoding the active kinase alone or in combination with coding sequences, such as a leader or secretory sequence (e.g., a pre-pro or pro-protein sequence), the sequence encoding the active kinase, with or without the additional coding sequences, plus additional non-coding sequences, for example introns and non-coding 5' and 3' sequences such as transcribed but non-translated sequences that play a role in transcription, mRNA processing (including splicing and polyadenylation signals), ribosome binding and stability of mRNA. In addition, the nucleic acid molecule may be fused to a marker sequence encoding, for example, a peptide that facilitates purification.

[0080] Isolated nucleic acid molecules can be in the form of RNA, such as mRNA, or in the form DNA, including cDNA and genomic DNA, obtained by cloning or produced by chemical synthetic techniques or by a combination thereof. The nucleic acid, especially DNA, can be double-stranded or single-stranded. Single-stranded nucleic acid can be the coding strand (sense strand) or the non-coding strand (anti-sense strand).

[0081] The invention further provides nucleic acid molecules that encode fragments of the peptides of the present invention and that encode obvious variants of the kinase proteins of the present invention that are described above. Such nucleic acid molecules may be naturally occurring, such as allelic variants (same locus), paralogs (different locus), and orthologs (different organism), or may be constructed by recombinant DNA methods or by chemical synthesis. Such non-naturally occurring variants may be made by mutagenesis techniques, including those applied to nucleic acid molecules, cells, or organisms. Accordingly, as discussed above, the variants can contain nucleotide substitutions, deletions, inversions and insertions. Variation can occur in either or both the coding and non-coding regions. The variations can produce both conservative and non-conservative amino acid substitutions.

[0082] According to certain embodiments of the present invention, mutations to HGFR are utilized. For example, the tyrosine at residue 12130 is replaced with cysteine [SEQ ID NO. 10; a germline mutation in HPRC]; the methionine 1250 at residue 1250 is replaced with threonine [SEQ ID NO. 11]; and/or the histidine at residue 1094 is replaced with

argenine [SEQ ID NO. 14].

SEQ ID NO. 10:

atggtccaca ttgacctcag tgctctaaat ccagagctgg tccaggcagt gcagcatgta
gtgattgggc ccagtagcct gattgtgcat ttcaatgaag tcataggaag agggcatttt
ggttgtgtat atcatgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg
aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc
atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt
gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt
cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc
aaagggatga aatatcttgc aagcaaaaag tttgtccaca gagacttggc tgcaagaaac
tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg
tgtgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg
atggctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt
ggcgtcgtcc tctgggagct gatgacaaga ggagccccac cttatcctga cgtaaacacc
tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca
gaccccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc
ttttctgaac tggtgtcccg gatatcagcg atcttctcta ctttcattgg ggagcac

SEQ ID NO 11:

atggtccaca ttgacctcag tgctctaaat ccagagctgg tccaggcagt gcagcatgta
gtgattgggc ccagtagcct gattgtgcat ttcaatgaag tcataggaag agggcatttt
ggttgtgtat atcatgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg
aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc
atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt
gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt
cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc
aaaggcatga aatatcttgc gagcaaaaag tttgtccaca gagacttggc tgcaagaaac
tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg
tatgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg
accgctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt
ggcgtgctcc tctgggagct gatgacaaga ggagccccac cttatcctga tgtaaacacc
tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca
gaccccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc
ttttctgaac tggtgtcccg gatatcagcg atcttctcta ctttcattgg ggagcac

SEQ ID NO 14:

atggtccaca ttgacctcag tgctctaaat ccagagctgg tccaggcagt gcagcatgta
gtgattgggc ccagtagcct gattgtgcat ttcaatgaag tcataggaag agggcatttt
ggttgtgtat atcgtgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg
aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc
atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt
gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt
cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc
aaagggatga aatatcttgc aagcaaaaag tttgtccaca gagacttggc tgcaagaaac
tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg
tatgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg
atggctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt
ggcgtcgtcc tctgggagct gatgacaaga ggagccccac cttatcctga cgtaaacacc
tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca
gaccccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc
ttttctgaac tggtgtcccg gatatcagcg atcttctcta ctttcattgg ggagcac

[0083] A fragment comprises a contiguous nucleotide sequence greater than about 8 or more nucleotides. Further, a fragment could be at least about 30, preferably at least about 40, more preferably at least about 50, and even more preferably at least about 100 or more nucleotides in length. The length of the fragment will be based on its intended use. For example, the fragment can encode epitope bearing regions of the peptide, or can be useful as DNA probes and primers. Such fragments can be isolated using the known nucleotide sequence to synthesize an oligonucleotide probe. A labeled probe can then be used to screen a cDNA library, genomic DNA library, or mRNA to isolate nucleic acid corresponding to the coding region. Further, primers can be used in PCR reactions to clone specific regions of gene.

[0084] A probe/primer typically comprises substantially a purified oligonucleotide or oligonucleotide pair. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or more consecutive nucleotides.

[0085] Orthologs, homologs, and allelic variants can be identified using methods known in the art. As described above, these variants comprise a nucleotide sequence encoding a peptide that is preferably about 60-65%, more preferably about 70-75%, and even more preferably at least about 90-95% or more homologous to the nucleotide sequence provided in SEQ ID NO: 1 or a fragment of this sequence. Such nucleic acid molecules can readily be identified as being able to hybridize under moderate to stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1 or a fragment of the sequence.

[0086] As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences encoding a peptide at least about 50%, and more preferably at least about 55% or more, homologous to each other typically remain hybridized to each other. The conditions can be such that sequences at least about 65%, preferably at least about 70%, and more preferably at least about 75% or more homologous to each other typically remains hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology,* John Wiley & Sons, N.Y., 6.3.1-6.3.6 (1989), which is hereby incorporated by reference in its entirety. One example of stringent hybridization conditions is hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65°C.

[0087] As used herein, the term "hybridizes under moderate conditions" is intended to describe conditions for hybridization and washing which are less severe than those described above for stringent conditions. Such moderate conditions are known to those skilled in the art and can be found in *Molecular Cloning, A laboratory manual,* J.Sambrook, E.F. Fritisch, T. Maniatis , Cold Spring Harbor Press Book 2 Chapter 9. One example of moderate conditions is hybridization in 6x SSC at room temperature, followed by 2x SSc and 0.1% SDS at 37°C.

[0088] The nucleic acid molecules of the present invention are useful for probes, primers, and chemical intermediates, and in biological assays. For example, the nucleic acid molecules can be used as hybridization probes for cDNA and genomic DNA to isolate full-length cDNA and genomic clones encoding the peptide described herein and to isolate cDNA and genomic clones that correspond to variants (alleles, orthologs, etc.) producing the same or related peptides described herein. The probe can correspond to any sequence along the entire length of the nucleic acid molecules provided in SEQ ID NO: 1. Accordingly, it could be derived from 5' noncoding regions, the coding region, and 3' non-

coding regions. However, as discussed, fragments are not to be construed as those which may encompass fragments disclosed prior to the present invention. Probes can be used as a part of a diagnostic test kit for identifying cells or tissues that express a kinase protein, such as by measuring a level of a receptor-encoding nucleic acid in a sample of cells from a subject e.g., mRNA or genomic DNA, or determining if a receptor gene has been mutated.

[0089] The nucleic acid molecules of the present invention are useful for producing peptides for use in crystallization studies, drug discovery, and drug design. The nucleic acid molecules are also useful as primers for PCR to amplify any given region of a nucleic acid molecule and are useful to synthesize anti-sense molecules of desired length and sequence. The nucleic acid molecules are also useful for constructing recombinant vectors. Such vectors include expression vectors that express a portion of, or all of, the peptide sequences. Vectors also include insertion vectors, used to integrate into another nucleic acid molecule sequence, such as into the cellular genome, to alter *in situ* expression of a gene and/or gene product. For example, an endogenous coding sequence can be replaced via homologous recombination with all or part of the coding region containing one or more specifically introduced mutations. In addition, the nucleic acid molecules are useful for expressing antigenic portions of the proteins; for determining the chromosomal positions of the nucleic acid molecules by means of *in situ* hybridization methods; for designing ribozymes corresponding to all, or a part, of the mRNA produced from the nucleic acid molecules described herein; for constructing host cells expressing a part, or all, of the nucleic acid molecules and peptides; for constructing transgenic animals expressing all, or a part, of the nucleic acid molecules and peptides; and for making vectors that express part, or all, of the peptides.

[0090] Further, the nucleic acid molecules are useful as hybridization probes for determining the presence, level, form and distribution of nucleic acid expression. Accordingly, the probes can be used to detect the presence of, or to determine levels of, a specific nucleic acid molecule in cells, tissues, and in organisms. The nucleic acid whose level is determined can be DNA or RNA. Accordingly, probes corresponding to the peptides described herein can be used to assess expression and/or gene copy number in a given cell, tissue, or organism. These uses are relevant for diagnosis of disorders involving an increase or decrease in kinase protein expression relative to normal results.

[0091] *In vitro* techniques for detection of mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detecting DNA include Southern hybridizations and *in situ* hybridization.

C. Vectors and Host Cells

[0092] The invention also provides vectors containing the nucleic acid molecules described herein. The term "vector" refers to a vehicle, preferably a nucleic acid molecule, that can transport the nucleic acid molecules. When the vector is a nucleic acid molecule, the nucleic acid molecules are covalently linked to the vector nucleic acid. With this aspect of the invention, the vector includes a plasmid, single or double stranded phage, a single or double stranded RNA or DNA viral vector, or artificial chromosome, such as a BAC, PAC, YAC, OR MAC. Various expression vectors can be used to express polynucleotides encoding an hHGFR kinase, such as (but not limited to) pET and pProEX. A vector can be maintained in the host cell as an extrachromosomal element where it replicates and produces additional copies of the nucleic acid molecules. Alternatively, the vector may integrate into the host cell genome and produce additional copies of the nucleic acid molecules when the host cell replicates. The invention provides vectors for the maintenance (cloning vectors) or vectors for expression (expression vectors) of the nucleic acid molecules. The vectors can function in prokaryotic or eukaryotic cells or in both (shuttle vectors).

[0093] Expression vectors contain cis-acting regulatory regions that are operably linked in the vector to the nucleic acid molecules such that transcription of the nucleic acid molecules is allowed in a host cell. The nucleic acid molecules can be introduced into the host cell with a separate nucleic acid molecule capable of affecting transcription. Thus, the second nucleic acid molecule may provide a trans-acting factor interacting with the cis-regulatory control region to allow transcription of the nucleic acid molecules from the vector. Alternatively, a trans-acting factor may be supplied by the host cell. Finally, a trans-acting factor can be produced from the vector itself. It is understood, however, that in some embodiments, transcription and/or translation of the nucleic acid molecules can occur in a cell-free system.

[0094] The regulatory sequence to which the nucleic acid molecules described herein can be operably linked include promoters for directing mRNA transcription. These include, but are not limited to, the left promoter from bacteriophage λ, the lac, TRP, and TAC promoters from E. *coli,* the early and late promoters from SV40, the CMV immediate early promoter, the adenovirus early and late promoters, and retrovirus long-terminal repeats. In addition to control regions that promote transcription, expression vectors may also include regions that modulate transcription, such as repressor binding sites and enhancers. Examples include the SV40 enhancer, the cytomegalovirus immediate early enhancer, polyoma enhancer, adenovirus enhancers, and retrovirus LTR enhancers. The term "operably linked" as used herein indicates that a gene and a regulatory sequence(s), such as a promoter, are connected in such a way as to permit gene expression when the appropriate molecules (e.g., transcriptional activator proteins or proteins which include transcriptional activation domains) are bound to the regulatory sequence(s).

[0095] In addition to containing sites for transcription initiation and control, expression vectors can also contain se-

quences necessary for transcription termination and, in the transcribed region, a ribosome binding site for translation. Other regulatory control elements for expression include initiation and termination codons as well as polyadenylation signals. The person of ordinary skill in the art would be aware of the numerous regulatory sequences that are useful in expression vectors. Such regulatory sequences are described, for example, in Sambrook et al., *Molecular Cloning: A Laboratory Manual.* 3rd. *ed.*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, (2001), which is hereby incorporated by reference in its entirety.

[0096] A variety of expression vectors can be used to express a nucleic acid molecule. Such vectors include chromosomal, episomal, and virus-derived vectors, for example vectors derived from bacterial plasmids, from bacteriophage, from yeast episomes, from yeast chromosomal elements, including yeast artificial chromosomes, from viruses such as baculoviruses, papovaviruses such as SV40, Vaccinia viruses, adenoviruses, poxviruses, pseudorabies viruses, and retroviruses. Vectors may also be derived from combinations of these sources such as those derived from plasmid and bacteriophage genetic elements, e.g., cosmids and phagemids. Appropriate cloning and expression vectors for prokaryotic and eukaryotic hosts are described in Sambrook et al., *supra.*

[0097] The regulatory sequence may provide constitutive expression in one or more host cells (i.e., tissue specific) or may provide for inducible expression in one or more cell types such as by temperature, nutrient additive, or exogenous factor such as a hormone or other ligand. A variety of vectors providing for constitutive and inducible expression in prokaryotic and eukaryotic hosts are known to those of ordinary skill in the art.

[0098] The nucleic acid molecules can be inserted into the vector nucleic acid by well-known methodology. Generally, the DNA sequence that will ultimately be expressed is joined to an expression vector by cleaving the DNA sequence and the expression vector with one or more restriction enzymes and then ligating the fragments together. Procedures for restriction enzyme digestion and ligation are known to those of ordinary skill in the art.

[0099] The vector containing the appropriate nucleic acid molecule can be introduced into an appropriate host cell for propagation or expression using techniques known to those of ordinary skill in the art. Bacterial cells include, but are not limited to, *E. coli, Streptomyces,* and *Salmonella typhimurium.* Eukaryotic cells include, but are not limited to, yeast, insect cells such as *Drosophila,* animal cells such as COS and CHO cells, and plant cells.

[0100] As described herein, it may be desirable to express a peptide of the present invention as a fusion protein. Accordingly, the invention provides fusion vectors that allow for the production of such peptides. Fusion vectors can increase the expression of a recombinant protein, increase the solubility of the recombinant protein, and aid in the purification of the protein by acting for example as a ligand for affinity purification. A proteolytic cleavage site may be introduced at the junction of the fusion moiety so that the desired peptide can ultimately be separated from the fusion moiety. Proteolytic enzymes include, but are not limited to, factor Xa, thrombin, and enterokinase. Typical fusion expression vectors include pGEX (Smith et al., *Gene* 67:31-40 (1988)), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein. Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann et al., *Gene* 69:301-315 (1988)) and pET 11d (Studier et al., *Gene Expression Technology: Methods in Enzymology* 185:60-89 (1990)).

[0101] Recombinant protein expression can be maximized in a host bacteria by providing a genetic background wherein the host cell has an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, S., *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California 119-128 (1990)). Alternatively, the sequence of the nucleic acid molecule of interest can be altered to provide preferential codon usage for a specific host cell, for example *E. coli.* (Wada et al., *Nucleic Acids Res.* 20:2111-2118 (1992)).

[0102] The nucleic acid molecules can also be expressed by expression vectors that are operative in yeast. Examples of vectors for expression in yeast, e.g., *S. cerevisiae*, include pYepSec1 (Baldari, et al., *EMBO J.* 6:229-234 (1987)), pMFa (Kurjan et al., *Cell* 30:933-943 (1982)), pJRY88 (Schultz et al., *Gene* 54:113-123 (1987)), and pYES2 (Invitrogen Corporation, San Diego, CA). The nucleic acid molecules can also be expressed in insect cells using, for example, baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series (Smith et al., *Mol. Cell Biol.* 3:2156-2165 (1983)) and the pVL series (Lucklow et al., *Virology* 170:31-39 (1989)). In certain embodiments of the invention, the nucleic acid molecules described herein are expressed in mammalian cells using mammalian expression vectors. Examples of mammalian expression vectors include pCDM8 (Seed, B., *Nature* 329:840 (1987)) and pMT2PC (Kaufman et al., *EMBO J.* 6:187-195 (1987)). Each of the foregoing references is hereby incorporated by reference in its entirety.

[0103] The expression vectors listed herein are provided by way of example only of the well-known vectors available to those of ordinary skill in the art that would be useful to express the nucleic acid molecules. Preferred vectors include pET28a (Novagen, Madison, WI), pAcSG2 (Pharmingen, San Diego, CA), and pFastBac (Life Technologies, Gaithersburg, MD). The person of ordinary skill in the art would be aware of other vectors suitable for maintenance propagation or expression of the nucleic acid molecules described herein. These are found, for example, in Sambrook et al., *supra.*

[0104] The invention also encompasses vectors in which the nucleic acid sequences described herein are cloned into the vector in reverse orientation, but operably linked to a regulatory sequence that permits transcription of anti-

sense RNA. Thus, an anti-sense transcript can be produced to all, or to a portion, of the nucleic acid molecule sequences described herein, including both coding and non-coding regions. Expression of this anti-sense RNA is subject to each of the parameters described above in relation to expression of the sense RNA (regulatory sequences, constitutive or inducible expression, tissue-specific expression).

[0105] The invention also relates to recombinant host cells containing the vectors described herein. Host cells therefore include prokaryotic cells, lower eukaryotic cells such as yeast, other eukaryotic cells such as insect cells, and higher eukaryotic cells such as mammalian cells. Preferred host cells of the instant invention include *E. coli* and Sf9.

[0106] The recombinant host cells are prepared by introducing the vector constructs described herein into the cells by techniques readily available to the person of ordinary skill in the art. These include, but are not limited to, calcium phosphate transfection, DEAE-dextran-mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, lipofection, and other techniques such as those found in Sambrook et al., *supra.*

[0107] Host cells can contain more than one vector. Thus, different nucleotide sequences can be introduced on different vectors of the same cell. Similarly, the nucleic acid molecules can be introduced either alone or with other nucleic acid molecules that are not related to the nucleic acid molecules such as those providing trans-acting factors for expression vectors. When more than one vector is introduced into a cell, the vectors can be introduced independently, co-introduced or joined to the nucleic acid molecule vector.

[0108] In the case of bacteriophage and viral vectors, these can be introduced into cells as packaged or encapsulated virus by standard procedures for infection and transduction. Viral vectors can be replication-competent or replication-defective. In the case in which viral replication is defective, replication will occur in host cells providing functions that complement the defects.

[0109] Vectors generally include selectable markers that enable the selection of the subpopulation of cells that contain the recombinant vector constructs. The marker can be contained in the same vector that contains the nucleic acid molecules described herein or may be on a separate vector. Markers include tetracycline or ampicillin-resistance genes for prokaryotic host cells and dihydrofolate reductase or neomycin resistance for eukaryotic host cells. However, any marker that provides selection for a phenotypic trait will be effective.

[0110] While the active protein kinases can be produced in bacteria, yeast, mammalian cells, and other cells under the control of the appropriate regulatory sequences, cell- free transcription and translation systems can also be used to produce these proteins using RNA derived from the DNA constructs described herein.

[0111] Where secretion of the peptide is desired, appropriate secretion signals are incorporated into the vector. The signal sequence can be endogenous to the peptides or heterologous to these peptides.

[0112] It is also understood that depending upon the host cell used for the recombinant production of the peptides described herein, the peptides can have various glycosylation patterns, depending upon the cell, or maybe non-glycosylated as when produced in bacteria. In addition, the peptides may include an initial modified methionine in some cases as a result of a host-mediated process.

[0113] The recombinant host cells expressing the peptides described herein have a variety of uses. First, the cells are useful for producing a kinase protein or peptide that can be further purified to produce desired amounts of kinase protein or fragments. Thus, host cells containing expression vectors are useful for peptide production. Host cells are also useful for conducting cell-based assays involving the kinase protein or kinase protein fragments. Thus, a recombinant host cell expressing a kinase polypeptide of the invention is useful for assaying compounds that stimulate or inhibit kinase protein function. Host cells are also useful for identifying kinase protein mutants in which these functions are affected. If the mutants naturally occur and give rise to a pathology, host cells containing the mutations are useful to assay compounds that have a desired effect on the mutant kinase protein (for example, stimulating or inhibiting function) which may not be indicated by their effect on the native kinase protein.

D. Crystallization and Computer Methods for Model Building and Drug Design

[0114] Crystals of the polypeptides of the invention or ligand complexes of such polypeptides can be grown by a number of techniques including batch crystallization, vapor diffusion (either by sitting drop or hanging drop) and by microdialysis. Seeding of the crystals in some instances is required to obtain X-ray quality crystals. Standard micro and/or macro seeding of crystals may therefore be used. The HGFR-Compound 1 complex can be prepared as described below in reference to Example 2.

[0115] Once a crystal of the present invention is grown, X-ray diffraction data can be collected. X-ray diffraction data collection can be obtained using, for example, a MAR imaging plate detector. Crystals can be characterized by using X-rays produced in a conventional source (such as a sealed tube or a rotating anode) or using a synchrotron source.

[0116] Data processing and reduction can be carried out using programs such as HKL, DENZO, and SCALEPACK (Otwinowski and Minor, 1997, *Meth. Enymol.* 276:307-326 (1997)). In addition, X-PLOR, (Bruger, X-PLOR v.3.1 Manual, New Haven: Yale University, (1993)) or Heavy (T. Terwilliger, Los Alamos National Laboratory) may be utilized for bulk solvent correction and B-factor scaling. Electron density maps can be calculated using SHARP (La Fortelle, E. D. and

Bricogne G., *Meth. Enzymol.* 276:472-494 (1997)) and SOLOMON. Molecular models can be built into this map using O (Jones, T. et al., *ACTA Crystallogr.* A47:110-119 (1991)), XTALVIEW (Scripps Research) or QUANTA96 (Accelrys, Inc. San Diego). Refinement can be done using XPLOR (Brunger, "X-PLOR:A System for X-ray Crystallography and NMR," Yale University Press, New Haven, Conn), using the free R-value to monitor the course of refinement.

[0117] Once the three-dimensional structure of a crystal comprising HGFR or an HGFR-complex is determined, a potential ligand (antagonist or agonist) is examined through the use of computer modeling using a docking program such as FelxiDock (Tripos, St. Louis, MO), GRAM (Medical Univ. Of South Carolina), DOCK3.5 and 4.0 (Univ. Calif. San Francisco), Glide (Schrödinger, Portland, OR), Gold (Cambridge Crystallographic Data Centre, UK), FLEX-X (BioSolveIT GmbH, Germany); AGDOCK (in-house software from Agouron Pharmaceuticals; Gehlhaar et al., *Chemistry & Biol.* 2:317-324), Hex (Ritchie, D and Kemp, G., *Proteins: Struct. Funct. & Genet.* 39:178-194), or AUTODOCK (Scripps Research Institute). This procedure can include computer fitting of potential ligands to the HGFR substrate-binding domain to ascertain how well the shape and the chemical structure of the potential ligand will complement or interfere with the HGFR substrate-binding domain (Bugg et al., *Scientific American* Dec.:92-98 (1993); West et al., *TIPS* 16:67-74 (1995)). Computer programs can also be employed to estimate the attraction, repulsion, and steric hindrance of the ligand to the HGFR binding domain. Generally the tighter the fit (e.g., the lower the steric hindrance, and/or the greater the attractive force) the more potent the potential drug will be since these properties are consistent with a tighter-binding constant.

[0118] "Binding domain" also referred to as "binding site", "binding pocket", "substrate-binding site," "catalytic domain," or "substrate-binding domain," refers to a region or regions of a molecule or molecular complex, that, as a result of its shape, can associate with another chemical entity or compound. Such regions are of significant utility in fields such as drug discovery. The association of natural ligands or substrates with binding pockets of their corresponding receptors or enzymes is the basis of many biological mechanisms of action. Similarly, many drugs exert their biological effects via an interaction with the binding pockets of a receptor or enzyme. Such interactions may occur with all or part of the binding pocket. An understanding of such interactions can lead to the design of drugs having more favorable and specific interactions with their target receptor or enzyme, and thus, improved biological effects. Therefore, information related to ligand binding with the HGFR substrate-binding site is valuable in designing potential modulators of HGFR. Further, the more specificity in the design of a potential drug the more likely that the drug will not interact with other similar proteins, thus, minimizing potential side effects due to unwanted cross interactions.

[0119] Initially, a potential ligand could be obtained by screening a random chemical library. A ligand selected in this manner could be then be systematically modified by computer-modeling programs until one or more promising potential ligands are identified. Such analysis has been shown to be effective in the development of HIV protease inhibitors (Larn et al., *Science* 263:380-384 (1994); Wlodawer et al., *Ann. Rev. Biochem.* 62:543-585 (1993); Appelt, *Perspectives in Drug Discovery and Design* 1:23-48 (1993); Erickson, *Perspectives in Drug Discovery and Design* 1: 109-128 (1993). Such computer modeling allows the selection of a finite number of rational chemical modifications, as opposed to the countless number of essentially random chemical modifications that could be made, and of which any one might lead to a useful drug. Each chemical modification requires additional chemical steps, which while being reasonable for the synthesis of a finite number of compounds, quickly becomes overwhelming if all possible modifications needed to be synthesized. Thus, through the use of the structure coordinates disclosed herein and computer modeling, a large number of these compounds can be rapidly screened on the computer monitor screen, and a few likely candidates can be determined without the laborious synthesis of untold numbers of compounds.

[0120] Once a potential ligand (agonist or antagonist) is identified it can be either selected from commercial libraries of compounds or alternatively the potential ligand may be synthesized *de novo.* As mentioned above, the *de novo* synthesis of one or even a relatively small group of specific compounds is reasonable in the art of drug design. The prospective drug can be tested in the binding assay exemplified below to test its ability to bind to the HGFR substrate-binding domain. The effect of the prospective drug on HGFR activity can also be determined using the assay described herein or other HGFR assays known in the art.

[0121] When a suitable compound is identified, a supplemental crystal can be grown which comprises a protein-ligand complex formed between the HGFR domain and the compound. Preferably the crystal effectively diffracts X-rays allowing the determination of the atomic coordinates of the protein-ligand complex to a resolution value of about 3.0 Å or less, more preferably about 2.0 Å or less. Molecular Replacement Analysis can be used to determine the three-dimensional structure of the supplemental crystal.

[0122] Molecular replacement involves using a known three-dimensional structure as a search model to determine the structure of an identical or closely related molecule or protein-ligand complex in a new crystal form. The measured X-ray diffraction properties of the new crystal are compared with those calculated from a search model structure to compute the position and orientation of the protein in the new crystal. Computer programs that can be used for this purpose include: X-PLOR, EPMR (Kissinger et al. *Acta Cryst.* D55:484-491 (1999)), ProLSQ and AMORE (J. Navaza, *Acta Crysrallographics ASO,* 157-163 (1994)). Once the position and orientation are known an electron density map can be calculated using the search model to provide X-ray phases. Thereafter, the electron density is inspected for

structural differences and the search model is modified to conform to the new structure. Using this approach, it is possible to use the claimed structure to solve the three-dimensional structures of any such HGFR polypeptide-ligand complex. Other computer programs that can be used to solve the structures of such HGFR crystals include X-site, QUANTA, INSIGHT, ARP/wARP, and ICM.

[0123] For all of the drug design strategies described herein further refinements to the structure of the drug will generally be necessary and can be made by the successive iterations of any and/or all of the steps provided by the aforementioned strategies.

[0124] Another aspect of the invention involves using the structure coordinates generated from the HGFR -ligand complex to generate a three-dimensional shape. This is achieved through the use of commercially available software that is capable of generating three-dimensional graphical representations of molecules or portions thereof from a set of structure coordinates.

[0125] It will be readily apparent to those of skill in the art that the numbering of amino acids in other isoforms of HGFR may be different than that set forth for herein. Corresponding amino acids in other isoforms of HGFR are easily identified by inspection of the amino acid sequences, for example, through the use of commercially available homology software programs.

[0126] The amino acids of the HGFR domain of the polypeptides of the invention are described herein and are defined by a set of structure coordinates set forth in Table 1. The terms "structure coordinates" or "atomic coordinates" refer to Cartesian coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of a protein or protein-ligand complex in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are then used to establish the positions of the individual atoms of the enzyme or enzyme complex.

Table 1

ATOM	1	CB	LEU	1062	-5.656	32.472	9.323	1.00	42.24		C
ANISOU	1	CB	LEU	1062	4988	5484	5576	-719	-875	457	C
ATOM	2	CG	LEU	1062	-4.343	31.747	9.028	1.00	45.82		C
ANISOU	2	CG	LEU	1062	6417	5073	5918	773	-2605	-523	C
ATOM	3	CD1	LEU	1062	-3.291	31.922	10.117	1.00	49.80		C
ANISOU	3	CD1	LEU	1062	6543	6638	5741	1783	-2327	-3085	C
ATOM	4	CD2	LEU	1062	-4.608	30.252	8.793	1.00	61.21		C
ANISOU	4	CD2	LEU	1062	8940	5485	8834	2	-3713	-1422	C
ATOM	5	C	LEU	1062	-4.927	34.835	9.088	1.00	32.29		C
ANISOU	5	C	LEU	1062	2270	5351	4646	198	-130	1309	C
ATOM	6	O	LEU	1062	-3.746	35.184	9.314	1.00	35.90		O
ANISOU	6	O	LEU	1062	3421	4477	5741	-1230	-770	879	O
ATOM	7	N	LEU	1062	-6.957	34.298	10.421	1.00	35.32		N
ANISOU	7	N	LEU	1062	2492	5438	5488	363	-111	3338	N
ATOM	8	CA	LEU	1062	-5.610	33.834	10.010	1.00	31.18		C
ANISOU	8	CA	LEU	1062	1961	4568	5319	-249	-1111	1419	C
ATOM	9	N	VAL	1063	-5.635	35.320	8.052	1.00	33.88		N
ANISOU	9	N	VAL	1063	4004	4197	4671	563	-652	829	N
ATOM	10	CA	VAL	1063	-4.971	36.369	7.245	1.00	37.92		C
ANISOU	10	CA	VAL	1063	4464	4071	5871	117	-1511	1514	C
ATOM	11	CB	VAL	1063	-5.771	36.763	6.002	1.00	40.52		C
ANISOU	11	CB	VAL	1063	5622	4212	5561	183	-1748	1365	C
ATOM	12	CG1	VAL	1063	-5.271	38.081	5.394	1.00	45.84		C
ANISOU	12	CG1	VAL	1063	5460	5756	6200	-558	-1740	2571	C
ATOM	13	CG2	VAL	1063	-5.720	35.689	4.922	1.00	49.72		C
ANISOU	13	CG2	VAL	1063	5692	6405	6795	826	-2035	-304	C
ATOM	14	C	VAL	1063	-4.710	37.538	8.200	1.00	39.48		C
ANISOU	14	C	VAL	1063	3451	5518	6030	-897	-1094	793	C
ATOM	15	O	VAL	1063	-3.699	38.229	8.177	1.00	40.62		O
ANISOU	15	O	VAL	1063	3403	5114	6917	-825	-1890	2272	O
ATOM	16	N	GLN	1064	-5.682	37.725	9.084	1.00	37.95		N

Table 1 (continued)

ANISOU	16	N	GLN	1064	3174	4947	6299	383	-1356	1245	N
ATOM	17	CA	GLN	1064	-5.705	38.664	10.170	1.00	39.27		C
ANISOU	17	CA	GLN	1064	4283	4277	6360	527	-858	1541	C
ATOM	18	CB	GLN	1064	-7.053	38.571	10.905	1.00	46.57		C
ANISOU	18	CB	GLN	1064	4345	5743	7608	867	-356	955	C
ATOM	23	C	GLN	1064	-4.558	38.406	11.133	1.00	35.57		C
ANISOU	23	C	GLN	1064	4284	3605	5627	-193	-745	1294	C
ATOM	24	O	GLN	1064	-3.767	39.306	11.437	1.00	45.66		O
ANISOU	24	O	GLN	1064	5423	2722	9203	389	-1986	262	O
ATOM	25	N	ALA	1065	-4.518	37.159	11.580	1.00	29.57		N
ANISOU	25	N	ALA	1065	3049	3646	4541	-263	-123	1171	N
ATOM	26	CA	ALA	1065	-3.497	36.787	12.549	1.00	29.84		C
ANISOU	26	CA	ALA	1065	3405	3848	4084	-976	-258	1486	C
ATOM	27	CB	ALA	1065	-3.687	35.306	12.883	1.00	32.47		
ANISOU	27	CB	ALA	1065	3146	3579	5612	-273	-333	1426	C
ATOM	28	C	ALA	1065	-2.089	37.054	12.067	1.00	25.87		C
ANISOU	28	C	ALA	1065	3124	3301	3403	-419	-315	292	C
ATOM	29	O	ALA	1065	-1.180	37.393	12.848	1.00	26.64		O
ANISOU	29	O	ALA	1065	2881	4358	2883	204	-198	17	O
ATOM	30	N	VAL	1066	-1.835	36.917	10.762	1.00	26.85		N
ANISOU	30	N	VAL	1066	2739	4255	3206	-70	-872	397	N
ATOM	31	CA	VAL	1066	-0.436	37.056	10.364	1.00	26.36		C
ANISOU	31	CA	VAL	1066	2950	3462	3605	287	-304	343	C
ATOM	32	CB	VAL	1066	-0.083	36.006	9.295	1.00	28.45		C
ANISOU	32	CB	VAL	1066	3464	3113	4233	-338	-285	-36	C
ATOM	33	CG1	VAL	1066	-0.453	34.603	9.772	1.00	36.19		C
ANISOU	33	CG1	VAL	1066	4167	3284	6301	-985	-1217	473	C
ATOM	34	CG2	VAL	1066	-0.769	36.395	7.984	1.00	30.30		C
ANISOU	34	CG2	VAL	1066	3985	3335	4193	907	-483	-732	C
ATOM	35	C	VAL	1066	-0.092	38.411	9.781	1.00	24.00		C
ANISOU	35	C	VAL	1066	2887	3186	3046	177	-724	-37	C
ATOM	36	O	VAL	1066	1.077	38.661	9.417	1.00	23.42		O
ANISOU	36	O	VAL	1066	3052	2885	2960	-124	-441	-920	O
ATOM	37	N	GLN	1067	-1.054	39.310	9.668	1.00	23.79		N
ANISOU	37	N	GLN	1067	3069	3328	2642	275	-1049	-182	N
ATOM	38	CA	GLN	1067	-0.829	40.504	8.828	1.00	25.42		C
ANISOU	38	CA	GLN	1067	3390	3279	2991	208	-1380	-72	C
ATOM	39	CB	GLN	1067	-2.099	41.362	8.853	1.00	32.36		C
ANISOU	39	CB	GLN	1067	3545	3823	4926	539	-1139	626	C
ATOM	40	CG	GLN	1067	-2.506	41.771	10.269	1.00	33.75		C
ANISOU	40	CG	GLN	1067	3125	4206	5494	982	-364	560	C
ATOM	41	CD	GLN	1067	-3.599	42.819	10.158	1.00	39.88		C
ANISOU	41	CD	GLN	1067	4158	4663	6334	1659	-406	1208	C
ATOM	42	OE1	GLN	1067	-3.432	43.710	9.330	1.00	52.77		O
ANISOU	42	OE1	GLN	1067	5684	5689	8676	1385	-832	2880	O
ATOM	43	NE2	GLN	1067	-4.650	42.688	10.963	1.00	38.22		N
ANISOU	43	NE2	GLN	1067	3384	4488	6650	1391	-621	-342	N
ATOM	44	C	GLN	1067	0.367	41.348	9.228	1.00	26.72		C
ANISOU	44	C	GLN	1067	3500	3686	2968	-132	-932	-91	C
ATOM	45	O	GLN	1067	0.971	41.896	8.291	1.00	30.88		O
ANISOU	45	O	GLN	1067	4066	4260	3409	-151	500	-870	O

Table 1 (continued)

ATOM	46	N	HIS	1068	0.749	41.488	10.490	1.00	22.49		N
ANISOU	46	N	HIS	1068	2696	2632	3219	765	-1235	-534	N
ATOM	47	CA	HIS	1068	1.878	42.369	10.817	1.00	20.79		C
ANISOU	47	CA	HIS	1068	2761	2235	2903	499	-528	-167	C
ATOM	48	CB	HIS	1068	1.599	43.204	12.077	1.00	24.08		C
ANISOU	48	CB	HIS	1068	2417	3415	3319	-294	-74	-938	C
ATOM	49	CG	HIS	1068	0.326	44.002	12.029	1.00	23.87		C
ANISOU	49	CG	HIS	1068	3189	3310	2570	239	-466	-1342	C
ATOM	50	CD2	HIS	1068	-0.836	43.766	12.720	1.00	24.71		C
ANISOU	50	CD2	HIS	1068	2664	3594	3129	683	-612	-1166	C
ATOM	51	ND1	HIS	1068	0.072	45.120	11.276	1.00	26.89		N
ANISOU	51	ND1	HIS	1068	3883	3106	3226	-228	-1210	-1263	N
ATOM	52	CE1	HIS	1068	-1.160	45.547	11.492	1.00	30.43		C
ANISOU	52	CE1	HIS	1068	3833	3687	4041	215	-1728	-845	C
ATOM	53	NE2	HIS	1068	-1.726	44.730	12.373	1.00	28.63		N
ANISOU	53	NE2	HIS	1068	3424	3481	3975	942	-928	-1207	N
ATOM	54	C	HIS	1068	3.158	41.560	11.002	1.00	21.05		C
ANISOU	54	C	HIS	1068	2589	1916	3491	168	-955	-173	C
ATOM	55	O	HIS	1068	4.155	42.094	11.526	1.00	21.33		O
ANISOU	55	O	HIS	1068	2663	2336	3105	-43	-627	-326	O
ATOM	56	N	VAL	1069	3.167	40.288	10.587	1.00	19.97		N
ANISOU	56	N	VAL	1069	2603	2209	2777	347	-611	-509	N
ATOM	57	CA	VAL	1069	4.419	39.516	10.717	1.00	19.24		C
ANISOU	57	CA	VAL	1069	2820	2362	2129	558	-190	143	C
ATOM	58	CB	VAL	1069	4.316	38.354	11.715	1.00	22.02		C
ANISOU	58	CB	VAL	1069	3642	2341	2384	308	-63	151	C
ATOM	59	CG1	VAL	1069	4.023	38.874	13.117	1.00	28.55		C
ANISOU	59	CG1	VAL	1069	5153	3362	2334	403	598	264	C
ATOM	60	CG2	VAL	1069	3.246	37.357	11.278	1.00	24.46		C
ANISOU	60	CG2	VAL	1069	3088	3407	2799	-232	-46	795	C
ATOM	61	C	VAL	1069	4.858	38.995	9.350	1.00	18.10		C
ANISOU	61	C	VAL	1069	2737	2084	2054	419	-635	-116	C
ATOM	62	O	VAL	1069	5.775	38.193	9.242	1.00	18.22		O
ANISOU	62	O	VAL	1069	2723	2181	2019	453	-330	170	O
ATOM	63	N	VAL	1070	4.215	39.458	8.266	1.00	19.19		N
ANISOU	63	N	VAL	1070	2697	2437	2157	385	-602	44	N
ATOM	64	CA	VAL	1070	4.619	39.011	6.944	1.00	19.24		C
ANISOU	64	CA	VAL	1070	2347	2944	2019	217	-469	136	C
ATOM	65	CB	VAL	1070	3.503	39.187	5.900	1.00	22.58		C
ANISOU	65	CB	VAL	1070	2536	3873	2170	58	-613	325	C
ATOM	66	CG1	VAL	1070	3.971	38.874	4.499	1.00	28.99		C
ANISOU	66	CG1	VAL	1070	3261	5784	1971	702	-704	513	C
ATOM	67	CG2	VAL	1070	2.330	38.275	6.266	1.00	24.98		C
ANISOU	67	CG2	VAL	1070	3104	3947	2440	-713	-721	-585	C
ATOM	68	C	VAL	1070	5.874	39.792	6.541	1.00	19.01		C
ANISOU	68	C	VAL	1070	2659	2193	2372	65	-559	75	C
ATOM	69	O	VAL	1070	5.982	41.014	6.711	1.00	24.45		O
ANISOU	69	O	VAL	1070	4066	2110	3114	249	-535	149	O
ATOM	70	N	ILE	1071	6.825	39.063	6.003	1.00	17.21		N
ANISOU	70	N	ILE	1071	2468	2035	2034	44	-406	676	N
ATOM	71	CA	ILE	1071	8.101	39.583	5.519	1.00	17.62		C

Table 1 (continued)

ANISOU	71	CA	ILE	1071	2679	2026	1989	-295	-480	388	C
ATOM	72	CB	ILE	1071	9.289	38.803	6.101	1.00	20.55		C
ANISOU	72	CB	ILE	1071	2449	2963	2398	-146	-535	340	C
ATOM	73	CG2	ILE	1071	10.570	39.163	5.366	1.00	24.19		C
ANISOU	73	CG2	ILE	1071	2854	2460	3876	178	188	899	C
ATOM	74	CG1	ILE	1071	9.381	38.973	7.635	1.00	21.09		C
ANISOU	74	CG1	ILE	1071	3261	2347	2407	-491	-1080	417	C
ATOM	75	CD1	ILE	1071	10.243	37.970	8.359	1.00	21.91		C
ANISOU	75	CD1	ILE	1071	3147	2946	2233	348	127	799	C
ATOM	76	C	ILE	1071	8.133	39.519	3.993	1.00	19.93		C
ANISOU	76	C	ILE	1071	3336	2256	1980	182	-104	412	C
ATOM	77	O	ILE	1071	7.976	38.429	3.412	1.00	21.78		O
ANISOU	77	O	ILE	1071	3638	2597	2039	-228	-477	213	O
ATOM	78	N	GLY	1072	8.324	40.654	3.328	1.00	20.86		N
ANISOU	78	N	GLY	1072	3232	2498	2196	246	-255	751	N
ATOM	79	CA	GLY	1072	8.367	40.662	1.868	1.00	24.04		C
ANISOU	79	CA	GLY	1072	3777	3106	2250	169	160	780	C
ATOM	80	C	GLY	1072	9.644	40.009	1.360	1.00	20.97		C
ANISOU	80	C	GLY	1072	3001	2894	2074	-549	-441	61	C
ATOM	81	O	GLY	1072	10.716	40.053	1.976	1.00	19.86		O
ANISOU	81	O	GLY	1072	3387	2343	1815	-788	-788	590	O
ATOM	82	N	PRO	1073	9.510	39.381	0.195	1.00	21.09		N
ANISOU	82	N	PRO	1073	3042	2647	2324	-460	-767	-114	N
ATOM	83	CD	PRO	1073	8.346	39.297	-0.664	1.00	26.42		C
ANISOU	83	CD	PRO	1073	3184	3883	2972	-309	-1038	-617	C
ATOM	84	CA	PRO	1073	10.659	38.651	-0.329	1.00	20.61		C
ANISOU	84	CA	PRO	1073	3246	2358	2227	-393	-649	95	C
ATOM	85	CB	PRO	1073	10.211	38.125	-1.706	1.00	24.26		C
ANISOU	85	CB	PRO	1073	3874	2924	2419	-259	-783	-305	C
ATOM	86	CG	PRO	1073	8.817	38.584	-1.906	1.00	29.68		C
ANISOU	86	CG	PRO	1073	3674	4569	3035	-339	-1211	-1081	C
ATOM	87	C	PRO	1073	11.867	39.551	-0.513	1.00	19.99		C
ANISOU	87	C	PRO	1073	3129	2452	2014	-290	-657	592	C
ATOM	88	O	PRO	1073	12.984	39.039	-0.367	1.00	23.20		O
ANISOU	88	O	PRO	1073	3174	2549	3093	-117	-902	-382	O
ATOM	89	N	ASER	1074	11.719	40.845	-0.828	0.50	21.38		N
ANISOU	89	N	ASER	1074	3775	2431	1919	-444	-1016	625	N
ATOM	90	N	BSER	1074	11.651	40.837	-0.819	0.50	20.89		N
ANISOU	90	N	BSER	1074	3635	2384	1917	-418	-1029	483	N
ATOM	91	CA	ASER	1074	12.963	41.605	-1.046	0.50	21.22		C
ANISOU	91	CA	ASER	1074	3769	2360	1933	-309	-825	840	C
ATOM	92	CA	BSER	1074	12.823	41.696	-1.057	0.50	21.96		C
ANISOU	92	CA	BSER	1074	3905	2426	2013	-537	-752	478	C
ATOM	93	CB	ASER	1074	12.713	42.890	-1.841	0.50	23.69		C
ANISOU	93	CB	ASER	1074	4389	2301	2312	-186	-719	878	C
ATOM	94	CB	BSER	1074	12.418	42.950	-1.842	0.50	23.74		C
ANISOU	94	CB	BSER	1074	4454	2561	2004	-530	-783	628	C
ATOM	95	OG	ASER	1074	11.826	43.718	-1.106	0.50	23.29		O
ANISOU	95	OG	ASER	1074	4566	2054	2230	-329	-972	514	O
ATOM	96	OG	BSER	1074	12.319	42.655	-3.234	0.50	23.49		O
ANISOU	96	OG	BSER	1074	4211	2616	2100	-301	-886	395	O

Table 1 (continued)

ATOM	97	C	ASER	1074	13.653	41.966	0.268	0.50	19.51		C
ANISOU	97	C	ASER	1074	3408	2037	1968	-397	-513	454	C
ATOM	98	C	BSER	1074	13.527	42.075	0.244	0.50	19.59		C
ANISOU	98	C	BSER	1074	3591	1874	1980	-594	-555	440	C
ATOM	99	O	ASER	1074	14.744	42.537	0.266	0.50	20.53		O
ANISOU	99	O	ASER	1074	3631	1737	2434	-552	-421	543	O
ATOM	100	O	BSER	1074	14.544	42.770	0.213	0.50	21.14		O
ANISOU	100	O	BSER	1074	3500	2093	2437	-616	-157	-2	O
ATOM	101	N	SER	1075	13.007	41.625	1.386	1.00	18.05		N
ANISOU	101	N	SER	1075	3116	1811	1930	-27	-533	486	N
ATOM	102	CA	SER	1075	13.591	41.840	2.704	1.00	16.60		C
ANISOU	102	CA	SER	1075	2940	1414	1953	-102	-570	254	C
ATOM	103	CB	SER	1075	12.504	42.149	3.723	1.00	20.80		C
ANISOU	103	CB	SER	1075	3261	2548	2094	635	-567	87	C
ATOM	104	OG	SER	1075	11.780	43.313	3.385	1.00	24.33		O
ANISOU	104	OG	SER	1075	2999	2848	3398	572	98	985	O
ATOM	105	C	SER	1075	14.363	40.604	3.154	1.00	17.00		C
ANISOU	105	C	SER	1075	2930	1658	1871	82	-579	154	C
ATOM	106	O	SER	1075	14.993	40.657	4.243	1.00	17.81		O
ANISOU	106	O	SER	1075	3173	1499	2094	-174	-825	321	O
ATOM	107	N	LEU	1076	14.373	39.491	2.418	1.00	16.66		N
ANISOU	107	N	LEU	1076	2809	1512	2010	53	-486	183	N
ATOM	108	CA	LEU	1076	14.914	38.246	2.961	1.00	16.17		C
ANISOU	108	CA	LEU	1076	2639	1649	1854	32	-286	289	C
ATOM	109	CB	LEU	1076	13.784	37.248	3.285	1.00	18.47		C
ANISOU	109	CB	LEU	1076	2876	1752	2390	-219	-595	467	C
ATOM	110	CG	LEU	1076	14.196	35.914	3.935	1.00	18.88		C
ANISOU	110	CG	LEU	1076	3203	1798	2175	-213	-481	477	C
ATOM	111	CD1	LEU	1076	14.861	36.139	5.283	1.00	18.69		C
ANISOU	111	CD1	LEU	1076	3510	1756	1834	-176	-228	480	C
ATOM	112	CD2	LEU	1076	12.962	35.021	4.014	1.00	19.42		C
ANISOU	112	CD2	LEU	1076	3376	1913	2088	-335	-104	519	C
ATOM	113	C	LEU	1076	15.835	37.577	1.999	1.00	17.58		C
ANISOU	113	C	LEU	1076	2935	1965	1781	424	-486	134	C
ATOM	114	O	LEU	1076	15.358	37.347	0.857	1.00	19.61		O
ANISOU	114	O	LEU	1076	3138	2208	2105	303	-705	-283	O
ATOM	115	N	ILE	1077	17.038	37.293	2.448	1.00	16.49		N
ANISOU	115	N	ILE	1077	2899	1747	1620	341	-334	308	N
ATOM	116	CA	ILE	1077	17.989	36.499	1.679	1.00	17.91		C
ANISOU	116	CA	ILE	1077	2927	1728	2150	330	-3	355	C
ATOM	117	CB	ILE	1077	19.315	37.249	1.550	1.00	19.48		C
ANISOU	117	CB	ILE	1077	3117	2014	2268	99	132	333	C
ATOM	118	CG2	ILE	1077	20.427	36.397	0.954	1.00	24.13		C
ANISOU	118	CG2	ILE	1077	2937	2291	3940	311	310	441	C
ATOM	119	CG1	ILE	1077	19.155	38.514	0.730	1.00	24.54		C
ANISOU	119	CG1	ILE	1077	3840	1863	3619	181	368	672	C
ATOM	120	CD1	ILE	1077	20.045	39.672	1.155	1.00	37.76		C
ANISOU	120	CD1	ILE	1077	6042	3146	5160	-1742	-416	1530	C
ATOM	121	C	ILE	1077	18.162	35.142	2.357	1.00	16.43		C
ANISOU	121	C	ILE	1077	2982	1620	1640	209	-301	61	C
ATOM	122	O	ILE	1077	18.505	35.125	3.554	1.00	20.58		O

Table 1 (continued)

ANISOU	122	O	ILE	1077	3818	2134	1869	160	-921	37	O
ATOM	123	N	VAL	1078	17.937	34.063	1.671	1.00	16.17		N
ANISOU	123	N	VAL	1078	2951	1684	1509	130	-255	111	N
ATOM	124	CA	VAL	1078	18.115	32.719	2.247	1.00	15.97		C
ANISOU	124	CA	VAL	1078	2765	1675	1629	147	-139	183	C
ATOM	125	CB	VAL	1078	16.869	31.839	2.048	1.00	17.27		C
ANISOU	125	CB	VAL	1078	2873	1638	2050	152	-117	101	C
ATOM	126	CG1	VAL	1078	17.032	30.506	2.816	1.00	19.12		C
ANISOU	126	CG1	VAL	1078	3317	1751	2196	14	-35	324	C
ATOM	127	CG2	VAL	1078	15.607	32.560	2.479	1.00	18.41		C
ANISOU	127	CG2	VAL	1078	2684	2246	2065	215	-259	-22	C
ATOM	128	C	VAL	1078	19.340	32.062	1.631	1.00	16.01		C
ANISOU	128	C	VAL	1078	2903	1693	1489	133	-52	162	C
ATOM	129	O	VAL	1078	19.470	31.991	0.386	1.00	18.40		O
ANISOU	129	O	VAL	1078	3189	2277	1524	150	-103	-36	O
ATOM	130	N	AHIS	1079	20.242	31.576	2.472	0.50	16.40		N
ANISOU	130	N	AHIS	1079	2797	1848	1587	253	-23	81	N
ATOM	131	N	BHIS	1079	20.261	31.553	2.440	0.50	16.51		N
ANISOU	131	N	BHIS	1079	2765	1870	1638	195	-94	52	N
ATOM	132	CA	AHIS	1079	21.430	30.839	2.028	0.50	17.26		C
ANISOU	132	CA	AHIS	1079	2998	1873	1687	359	10	-92	C
ATOM	133	CA	BHIS	1079	21.423	30.842	1.894	0.50	17.62		C
ANISOU	133	CA	BHIS	1079	2873	1936	1885	236	-56	-113	C
ATOM	134	CB	AHIS	1079	22.609	31.159	2.920	0.50	19.02		C
ANISOU	134	CB	AHIS	1079	2578	2285	2363	-268	87	509	C
ATOM	135	CB	BHIS	1079	22.676	31.237	2.653	0.50	18.95		C
ANISOU	135	CB	BHIS	1079	2648	2301	2253	-231	33	566	C
ATOM	136	CG	AHIS	1079	22.965	32.591	3.166	0.50	22.35		C
ANISOU	136	CG	AHIS	1079	3565	2384	2542	-618	-354	607	C
ATOM	137	CG	BHIS	1079	22.964	32.700	2.506	0.50	24.20		C
ANISOU	137	CG	BHIS	1079	3723	2499	2973	-792	-78	599	C
ATOM	138	CD2AHIS		1079	23.938	33.368	2.626	0.50	26.85		C
ANISOU	138	CD2AHIS		1079	4255	2688	3257	-1127	-63	545	C
ATOM	139	CD2BHIS		1079	23.498	33.364	1.459	0.50	25.31		C
ANISOU	139	CD2BHIS		1079	4723	2566	2328	-709	-1039	1229	C
ATOM	140	ND1AHIS		1079	22.316	33.420	4.042	0.50	24.01		N
ANISOU	140	ND1AHIS		1079	4560	2121	2443	-751	-239	487	N
ATOM	141	ND1BHIS		1079	22.699	33.635	3.478	0.50	25.67		N
ANISOU	141	ND1BHIS		1079	4025	2397	3332	-1141	-218	316	N
ATOM	142	CE1AHIS		1079	22.844	34.627	4.053	0.50	24.86		C
ANISOU	142	CE1AHIS		1079	4407	2522	2518	-1179	-730	371	C
ATOM	143	CE1BHIS		1079	23.066	34.827	3.037	0.50	27.09		C
ANISOU	143	CE1BHIS		1079	4668	2395	3230	-872	-884	828	C
ATOM	144	NE2AHIS		1079	23.854	34.620	3.182	0.50	27.29		N
ANISOU	144	NE2AHIS		1079	4446	2629	3293	-1071	-399	589	N
ATOM	145	NE2BHIS		1079	23.553	34.684	1.820	0.50	26.51		N

Table 1 (continued)

ANISOU	145	NE2BHIS		1079	4897	2558	2616	-722	-1431	1250	N
ATOM	146	C	AHIS	1079	21.048	29.364	2.013	0.50	17.00		C
ANISOU	146	C	AHIS	1079	2948	1929	1583	279	9	-102	C
ATOM	147	C	BHIS	1079	21.164	29.347	1.955	0.50	16.82		C
ANISOU	147	C	BHIS	1079	2883	1939	1567	227	3	-32	C
ATOM	148	O	AHIS	1079	21.161	28.669	3.030	0.50	16.03		O
ANISOU	148	O	AHIS	1079	2408	1917	1765	223	-196	-50	O
ATOM	149	O	BHIS	1079	21.480	28.687	2.946	0.50	17.29		O
ANISOU	149	O	BHIS	1079	3081	2034	1454	718	227	-161	O
ATOM	150	N	PHE	1080	20.579	28.836	0.882	1.00	17.39		N
ANISOU	150	N	PHE	1080	2954	2085	1568	147	99	-187	N
ATOM	151	CA	PHE	1080	20.081	27.430	0.904	1.00	16.92		C
ANISOU	151	CA	PHE	1080	2460	2201	1769	113	247	-233	C
ATOM	152	CB	PHE	1080	19.147	27.213	-0.304	1.00	18.38		C
ANISOU	152	CB	PHE	1080	2637	2391	1955	-124	55	38	C
ATOM	153	CG	PHE	1080	17.754	27.797	-0.090	1.00	17.89		C
ANISOU	153	CG	PHE	1080	2753	2269	1773	17	-128	-72	C
ATOM	154	CD1	PHE	1080	16.828	27.160	0.729	1.00	20.14		C
ANISOU	154	CD1	PHE	1080	2675	2920	2059	79	116	31	C
ATOM	155	CD2	PHE	1080	17.379	28.984	-0.711	1.00	19.48		C
ANISOU	155	CD2	PHE	1080	3443	1989	1971	203	-99	-384	C
ATOM	156	CE1	PHE	1080	15.561	27.654	0.948	1.00	21.11		C
ANISOU	156	CE1	PHE	1080	2562	3022	2436	106	-172	60	C
ATOM	157	CE2	PHE	1080	16.101	29.489	-0.510	1.00	19.43		C
ANISOU	157	CE2	PHE	1080	3349	2023	2012	247	-336	-589	C
ATOM	158	CZ	PHE	1080	15.197	28.833	0.312	1.00	22.31		C
ANISOU	158	CZ	PHE	1080	2990	2438	3047	-23	-387	-282	C
ATOM	159	C	PHE	1080	21.182	26.387	0.943	1.00	16.85		C
ANISOU	159	C	PHE	1080	2541	2090	1770	65	292	-117	C
ATOM	160	O	PHE	1080	20.882	25.213	1.136	1.00	20.88		O
ANISOU	160	O	PHE	1080	3183	2038	2713	14	531	-141	O
ATOM	161	N	ASN	1081	22.439	26.760	0.786	1.00	16.77		N
ANISOU	161	N	ASN	1081	2418	2420	1535	126	75	-223	N
ATOM	162	CA	ASN	1081	23.563	25.841	0.950	1.00	18.90		C
ANISOU	162	CA	ASN	1081	2641	2753	1789	387	47	-362	C
ATOM	163	CB	ASN	1081	24.627	26.074	-0.125	1.00	21.87		C
ANISOU	163	CB	ASN	1081	2589	3368	2353	507	327	-140	C
ATOM	164	CG	ASN	1081	24.146	25.632	-1.496	1.00	24.19		C
ANISOU	164	CG	ASN	1081	3816	3383	1991	258	590	-17	C
ATOM	165	OD1	ASN	1081	24.726	26.169	-2.454	1.00	29.42		O
ANISOU	165	OD1	ASN	1081	3861	4794	2524	356	1052	397	O
ATOM	166	ND2	ASN	1081	23.177	24.733	-1.679	1.00	24.15		N
ANISOU	166	ND2	ASN	1081	4914	2433	1831	227	260	-254	N
ATOM	167	C	ASN	1081	24.180	25.968	2.342	1.00	19.43		C
ANISOU	167	C	ASN	1081	2956	2350	2075	577	-300	-435	C
ATOM	168	O	ASN	1081	25.172	25.284	2.598	1.00	19.66		O
ANISOU	168	O	ASN	1081	2514	2746	2210	437	-132	-400	O
ATOM	169	N	AGLU	1082	23.593	26.803	3.196	0.50	16.40		N
ANISOU	169	N	AGLU	1082	2643	1940	1647	124	-72	-111	N
ATOM	170	N	BGLU	1082	23.633	26.800	3.230	0.50	16.73		N
ANISOU	170	N	BGLU	1082	2713	1981	1663	177	-98	-123	N

Table 1 (continued)

ATOM	171	CA	AGLU	1082	24.002	26.914	4.590	0.50	18.05		C
ANISOU	171	CA	AGLU	1082	2915	2211	1731	-217	-228	-59	C
ATOM	172	CA	BGLU	1082	24.117	26.915	4.602	0.50	18.05		C
ANISOU	172	CA	BGLU	1082	2897	2200	1762	-201	-244	-68	C
ATOM	173	CB	AGLU	1082	24.268	28.368	4.942	0.50	20.25		C
ANISOU	173	CB	AGLU	1082	3181	2425	2089	-548	-351	-252	C
ATOM	174	CB	BGLU	1082	24.411	28.355	4.980	0.50	20.64		C
ANISOU	174	CB	BGLU	1082	3301	2389	2151	-559	-283	-215	C
ATOM	175	CG	AGLU	1082	25.527	28.908	4.279	0.50	24.08		C
ANISOU	175	CG	AGLU	1082	3025	3060	3065	-848	-417	-116	C
ATOM	176	CG	BGLU	1082	25.566	29.068	4.328	0.50	24.46		C
ANISOU	176	CG	BGLU	1082	3148	3101	3045	-1017	-213	-477	C
ATOM	177	CD	AGLU	1082	25.698	30.368	4.642	0.50	24.26		C
ANISOU	177	CD	AGLU	1082	2477	3138	3602	-840	-315	-386	C
ATOM	178	CD	BGLU	1082	26.921	28.451	4.590	0.50	28.74		C
ANISOU	178	CD	BGLU	1082	3299	3660	3962	-662	-192	-512	C
ATOM	179	OE1AGLU		1082	25.478	30.696	5.818	0.50	31.54		O1-
ANISOU	179	OE1AGLU		1082	3548	3995	4440	-926	857	-1176	O1-
ATOM	180	OE1BGLU		1082	27.156	27.855	5.662	0.50	31.80		O1-
ANISOU	180	OE1BGLU		1082	4268	2629	5187	-603	-805	44	O1-
ATOM	181	OE2AGLU		1082	26.045	31.170	3.770	0.50	28.09		O
ANISOU	181	OE2AGLU		1082	3921	2887	3863	-344	-1290	353	O
ATOM	182	OE2BGLU		1082	27.771	28.572	3.676	0.50	37.61		O
ANISOU	182	OE2BGLU		1082	3296	6069	4925	-868	347	-874	O
ATOM	183	C	AGLU	1082	22.927	26.322	5.485	0.50	17.58		C
ANISOU	183	C	AGLU	1082	3158	1863	1658	88	-36	-22	C
ATOM	184	C	BGLU	1082	23.076	26.333	5.556	0.50	17.03		C
ANISOU	184	C	BGLU	1082	2990	1850	1630	47	-106	-192	C
ATOM	185	O	AGLU	1082	22.025	26.997	5.975	0.50	16.90		O
ANISOU	185	0	AGLU	1082	3084	1731	1606	46	-135	5	O
ATOM	186	O	BGLU	1082	22.306	27.084	6.160	0.50	20.02		O
ANISOU	186	O	BGLU	1082	3596	2197	1814	490	131	-61	O
ATOM	187	N	VAL	1083	23.070	25.010	5.667	1.00	18.03		N
ANISOU	187	N	VAL	1083	2939	1936	1975	225	-167	174	N
ATOM	188	CA	VAL	1083	22.058	24.288	6.443	1.00	17.39		C
ANISOU	188	CA	VAL	1083	3290	1673	1645	306	262	-167	C
ATOM	189	CB	VAL	1083	21.922	22.854	5.916	1.00	24.18		C
ANISOU	189	CB	VAL	1083	4950	1903	2336	-349	296	-475	C
ATOM	190	CG1	VAL	1083	20.887	22.035	6.690	1.00	27.10		C
ANISOU	190	CG1	VAL	1083	5156	2112	3029	-643	692	-795	C
ATOM	191	CG2	VAL	1083	21.556	22.897	4.434	1.00	26.37		C
ANISOU	191	CG2	VAL	1083	3906	3775	2338	-430	344	-1262	C
ATOM	192	C	VAL	1083	22.435	24.282	7.905	1.00	17.65		C
ANISOU	192	C	VAL	1083	2873	2047	1787	522	63	-188	C
ATOM	193	O	VAL	1083	23.521	23.861	8.266	1.00	21.70		O
ANISOU	193	O	VAL	1083	2950	2986	2310	770	292	705	0
ATOM	194	N	ILE	1084	21.516	24.737	8.741	1.00	16.13		N
ANISOU	194	N	ILE	1084	2806	1743	1579	73	216	-40	N

Table 1 (continued)

ATOM	195	CA	ILE	1084	21.807	24.825	10.170	1.00	14.78		C
ANISOU	195	CA	ILE	1084	2425	1560	1630	63	1	47	C
ATOM	196	CB	ILE	1084	21.807	26.300	10.623	1.00	15.08		C
ANISOU	196	CB	ILE	1084	2611	1517	1603	-103	-60	134	C
ATOM	197	CG2	ILE	1084	23.007	26.993	10.035	1.00	20.31		C
ANISOU	197	CG2	ILE	1084	3149	2256	2312	-725	617	-578	C
ATOM	198	CG1	ILE	1084	20.506	27.059	10.305	1.00	15.80		C
ANISOU	198	CG1	ILE	1084	3022	1380	1601	163	-227	50	C
ATOM	199	CD1	ILE	1084	20.476	28.498	10.796	1.00	15.53		C
ANISOU	199	CD1	ILE	1084	3136	1428	1337	-19	-262	14	C
ATOM	200	C	ILE	1084	20.802	24.010	10.972	1.00	14.27		C
ATOM	201	O	ILE	1084	20.741	24.062	12.181	1.00	17.54		O
ANISOU	201	O	ILE	1084	3270	1960	1433	92	-110	220	O
ATOM	202	N	GLY	1085	19.960	23.213	10.295	1.00	16.41		N
ANISOU	202	N	GLY	1085	3083	1207	1944	-198	-352	274	N
ATOM	203	CA	GLY	1085	19.044	22.286	11.019	1.00	15.32		C
ANISOU	203	CA	GLY	1085	2520	1655	1646	-123	-130	-17	C
ATOM	204	C	GLY	1085	18.370	21.449	9.935	1.00	14.73		C
ANISOU	204	C	GLY	1085	2698	1443	1455	-126	12	22	C
ATOM	205	O	GLY	1085	18.127	21.918	8.815	1.00	16.10		O
ANISOU	205	O	GLY	1085	2935	1677	1505	205	-126	7	O
ATOM	206	N	ARG	1086	18.060	20.206	10.247	1.00	17.64		N
ANISOU	206	N	ARG	1086	3312	1330	2059	-90	-38	-65	N
ATOM	207	CA	ARG	1086	17.406	19.344	9.242	1.00	17.42		C
ANISOU	207	CA	ARG	1086	3021	1287	2313	172	-113	-293	C
ATOM	208	CB	ARG	1086	18.364	18.297	8.682	1.00	22.28		C
ANISOU	208	CB	ARG	1086	3468	1802	3196	540	31	-684	C
ATOM	209	CG	ARG	1086	19.674	18.872	8.120	1.00	29.91		C
ANISOU	209	CG	ARG	1086	3963	2412	4991	833	1200	-221	C
ATOM	210	CD	ARG	1086	20.619	17.705	7.779	1.00	40.67		C
ANISOU	210	CD	ARG	1086	4824	4062	6569	1782	1725	-1122	C
ATOM	211	NE	ARG	1086	21.926	18.207	7.327	1.00	43.96		N
ANISOU	211	NE	ARG	1086	4898	5021	6784	1621	1993	-1342	N
ATOM	212	CZ	ARG	1086	22.036	18.516	6.023	1.00	47.16		C
ANISOU	212	CZ	ARG	1086	5928	4990	7000	731	1928	-878	C
ATOM	213	NH1	ARG	1086	20.931	18.330	5.293	1.00	44.75		N1+
ANISOU	213	NH1	ARG	1086	6568	3804	6630	-216	1733	-274	N1+
ATOM	214	NH2	ARG	1086	23.150	18.978	5.488	1.00	44.27		N
ANISOU	214	NH2	ARG	1086	6041	3106	7674	752	1478	103	N
ATOM	215	C	ARG	1086	16.177	18.761	9.933	1.00	17.19		C
ANISOU	215	C	ARG	1086	3285	1237	2009	16	-169	-58	C
ATOM	216	O	ARG	1086	16.315	18.095	10.977	1.00	22.86		O
ANISOU	216	O	ARG	1086	3969	1937	2780	38	-359	713	O
ATOM	217	N	GLY	1087	15.007	18.996	9.400	1.00	18.31		N
ANISOU	217	N	GLY	1087	3157	1959	1842	-293	-68	66	N
ATOM	218	CA	GLY	1087	13.741	18.509	9.873	1.00	20.31		C
ANISOU	218	CA	GLY	1087	3473	2621	1622	-927	-181	19	C
ATOM	219	C	GLY	1087	13.052	17.627	8.859	1.00	21.07		C
ANISOU	219	C	GLY	1087	3779	2560	1666	-818	-73	-218	C
ATOM	220	O	GLY	1087	13.523	17.538	7.734	1.00	26.79		O
ANISOU	220	O	GLY	1087	4866	3372	1940	-1021	403	-608	O

Table 1 (continued)

ATOM	221	N	HIS	1088	11.974	16.990	9.231	1.00	24.91		N
ANISOU	221	N	HIS	1088	4177	3355	1930	-1526	-177	-459	N
ATOM	222	CA	HIS	1088	11.174	16.158	8.326	1.00	27.00		C
ANISOU	222	CA	HIS	1088	4895	2928	2436	-1464	-413	-654	C
ATOM	223	CB	HIS	1088	10.283	15.232	9.183	1.00	32.58		C
ANISOU	223	CB	HIS	1088	5242	2763	4373	-1747	-240	-82	C
ATOM	224	CG	HIS	1088	9.353	14.421	8.338	1.00	38.61		C
ANISOU	224	CG	HIS	1088	5086	4382	5204	-2254	433	-1268	C
ATOM	225	CD2	HIS	1088	9.506	13.244	7.716	1.00	42.66		C
ANISOU	225	CD2	HIS	1088	5506	4958	5745	-2299	282	-2026	C
ATOM	226	ND1	HIS	1088	8.066	14.836	8.050	1.00	36.87		N
ANISOU	226	ND1	HIS	1088	4674	4633	4703	-2762	693	-1056	N
ATOM	227	CE1	HIS	1088	7.453	13.943	7.282	1.00	41.93		C
ANISOU	227	CE1	HIS	1088	5515	5480	4938	-2234	305	-2015	C
ATOM	228	NE2	HIS	1088	8.321	12.972	7.074	1.00	45.01		N
ANISOU	228	NE2	HIS	1088	6037	6002	5064	-1683	-231	-2354	N
ATOM	229	C	HIS	1088	10.388	17.034	7.376	1.00	26.78		C
ANISOU	229	C	HIS	1088	4785	3207	2183	-1394	-586	-907	C
ATOM	230	O	HIS	1088	10.230	16.763	6.187	1.00	31.07		O
ANISOU	230	O	HIS	1088	5705	3986	2115	-1251	-463	-961	O
ATOM	231	N	PHE	1089	9.865	18.160	7.886	1.00	26.90		N
ANISOU	231	N	PHE	1089	4805	3450	1966	-1068	-112	-545	N
ATOM	232	CA	PHE	1089	8.942	18.987	7.088	1.00	29.25		C
ANISOU	232	CA	PHE	1089	3618	4246	3252	-1186	5	-52	C
ATOM	233	CB	PHE	1089	7.917	19.633	8.033	1.00	36.34		C
ANISOU	233	CB	PHE	1089	4195	6183	3428	-427	358	74	C
ATOM	234	CG	PHE	1089	7.082	18.497	8.654	1.00	43.24		C
ANISOU	234	CG	PHE	1089	4275	7650	4504	-619	935	1061	C
ATOM	235	CD1	PHE	1089	7.541	17.686	9.681	1.00	43.64		C
ANISOU	235	CD1	PHE	1089	4510	7517	4553	-662	1001	1135	C
ATOM	236	CD2	PHE	1089	5.809	18.256	8.175	1.00	47.16		C
ANISOU	236	CD2	PHE	1089	4148	7847	5925	-764	766	1789	C
ATOM	237	CE1	PHE	1089	6.817	16.657	10.241	1.00	41.41		C
ANISOU	237	CE1	PHE	1089	4062	7287	4386	-378	1386	755	C
ATOM	238	CE2	PHE	1089	5.074	17.235	8.723	1.00	47.41		C
ANISOU	238	CE2	PHE	1089	4067	8514	5433	-633	1203	2104	C
ATOM	239	CZ	PHE	1089	5.553	16.435	9.736	1.00	44.74		C
ANISOU	239	CZ	PHE	1089	3958	8168	4873	-400	1249	1517	C
ATOM	240	C	PHE	1089	9.731	19.982	6.241	1.00	25.55		C
ANISOU	240	C	PHE	1089	3424	2951	3334	-675	-157	-233	C
ATOM	241	O	PHE	1089	9.219	20.500	5.250	1.00	27.22		O
ANISOU	241	O	PHE	1089	3389	3627	3324	-282	-25	-117	O
ATOM	242	N	GLY	1090	10.983	20.211	6.663	1.00	24.18		N
ANISOU	242	N	GLY	1090	3300	2739	3149	-537	39	-268	N
ATOM	243	CA	GLY	1090	11.847	21.203	6.055	1.00	23.73		C
ANISOU	243	CA	GLY	1090	2849	2964	3203	-134	-306	549	C
ATOM	244	C	GLY	1090	13.161	21.340	6.786	1.00	19.57		C
ANISOU	244	C	GLY	1090	3470	1938	2028	-485	-407	-24	C
ATOM	245	O	GLY	1090	13.348	20.827	7.875	1.00	25.58		O
ANISOU	245	O	GLY	1090	3696	3588	2436	-426	-167	944	O
ATOM	246	N	CYS	1091	14.109	22.041	6.175	1.00	19.42		N

Table 1 (continued)

ANISOU	246	N	CYS	1091	3428	1834	2116	-572	-653	258	N
ATOM	247	CA	CYS	1091	15.373	22.343	6.817	1.00	17.64		C
ANISOU	247	CA	CYS	1091	3299	1566	1837	-219	-515	4	C
ATOM	248	CB	CYS	1091	16.567	22.051	5.895	1.00	20.05		C
ANISOU	248	CB	CYS	1091	3493	2093	2031	-44	-430	-411	C
ATOM	249	SG	CYS	1091	16.694	20.266	5.604	1.00	30.65		S
ANISOU	249	SG	CYS	1091	6394	2454	2796	968	-663	-835	S
ATOM	250	C	CYS	1091	15.368	23.804	7.291	1.00	17.15		C
ANISOU	250	C	CYS	1091	3197	1589	1730	-74	-582	34	C
ATOM	251	O	CYS	1091	14.496	24.577	6.875	1.00	16.97		O
ANISOU	251	O	CYS	1091	2763	1788	1898	32	-305	43	O
ATOM	252	N	VAL	1092	16.345	24.075	8.153	1.00	16.59		N
ANISOU	252	N	VAL	1092	3244	1473	1588	-269	-581	198	N
ATOM	253	CA	VAL	1092	16.601	25.407	8.647	1.00	15.83		C
ANISOU	253	CA	VAL	1092	2994	1441	1580	-199	-431	168	C
ATOM	254	CB	VAL	1092	16.792	25.461	10.164	1.00	15.56		C
ANISOU	254	CB	VAL	1092	2766	1575	1572	-125	-170	-29	C
ATOM	255	CG1	VAL	1092	16.789	26.919	10.637	1.00	16.56		C
ANISOU	255	CG1	VAL	1092	3357	1410	1525	248	-162	182	C
ATOM	256	CG2	VAL	1092	15.719	24.682	10.891	1.00	16.19		C
ANISOU	256	CG2	VAL	1092	2466	1933	1751	-58	-368	326	C
ATOM	257	C	VAL	1092	17.864	25.906	7.945	1.00	14.33		C
ANISOU	257	C	VAL	1092	2817	1305	1321	-11	-508	48	C
ATOM	258	O	VAL	1092	18.877	25.175	7.918	1.00	16.95		O
ANISOU	258	O	VAL	1092	3252	1416	1772	306	-217	41	O
ATOM	259	N	TYR	1093	17.816	27.112	7.390	1.00	15.58		N
ANISOU	259	N	TYR	1093	3167	1295	1456	122	-89	136	N
ATOM	260	CA	TYR	1093	18.930	27.678	6.650	1.00	16.16		C
ANISOU	260	CA	TYR	1093	3015	1522	1602	101	-136	183	C
ATOM	261	CB	TYR	1093	18.536	27.951	5.187	1.00	15.50		C
ANISOU	261	CB	TYR	1093	2732	1745	1412	179	36	-14	C
ATOM	262	CG	TYR	1093	18.038	26.704	4.475	1.00	16.97		C
ANISOU	262	CG	TYR	1093	2938	1839	1670	9	64	-75	C
ATOM	263	CD1	TYR	1093	18.944	25.830	3.878	1.00	15.90		C
ANISOU	263	CD1	TYR	1093	3007	1572	1463	175	-174	74	C
ATOM	264	CE1	TYR	1093	18.471	24.699	3.232	1.00	18.28		C
ANISOU	264	CE1	TYR	1093	3439	1850	1658	-266	289	-113	C
ATOM	265	CD2	TYR	1093	16.672	26.404	4.405	1.00	17.46		C
ANISOU	265	CD2	TYR	1093	2990	1793	1852	-185	252	-45	C
ATOM	266	CE2	TYR	1093	16.224	25.271	3.758	1.00	19.35		C
ANISOU	266	CE2	TYR	1093	3238	2177	1937	-47	-322	-340	C
ATOM	267	CZ	TYR	1093	17.123	24.411	3.168	1.00	18.75		C
ANISOU	267	CZ	TYR	1093	3484	1933	1705	-308	23	-237	C
ATOM	268	OH	TYR	1093	16.694	23.277	2.521	1.00	23.14		O
ANISOU	268	OH	TYR	1093	4049	2391	2351	-564	57	-798	O
ATOM	269	C	TYR	1093	19.379	29.003	7.220	1.00	14.74		C
ANISOU	269	C	TYR	1093	2748	1556	1298	153	38	157	C
ATOM	270	O	TYR	1093	18.558	29.723	7.797	1.00	15.45		O
ANISOU	270	O	TYR	1093	2673	1544	1652	161	95	200	O
ATOM	271	N	HIS	1094	20.658	29.333	7.063	1.00	15.95		N
ANISOU	271	N	HIS	1094	2687	1595	1779	232	-53	-4	N

Table 1 (continued)

ATOM	272	CA	HIS	1094	21.106	30.675	7.400	1.00	14.41		C
ANISOU	272	CA	HIS	1094	2397	1538	1540	360	137	-113	C
ATOM	273	CB	HIS	1094	22.615	30.781	7.241	1.00	17.27		C
ANISOU	273	CB	HIS	1094	2202	2042	2318	464	-119	-180	C
ATOM	274	CG	HIS	1094	23.180	31.996	7.879	1.00	23.52		C
ANISOU	274	CG	HIS	1094	3006	2472	3458	-266	-129	-343	C
ATOM	275	CD2	HIS	1094	22.660	32.992	8.647	1.00	28.73		C
ANISOU	275	CD2	HIS	1094	3606	2741	4568	-125	-1100	-1414	C
ATOM	276	ND1	HIS	1094	24.497	32.314	7.755	1.00	36.95		N
ANISOU	276	ND1	HIS	1094	3184	4394	6461	-831	-465	-1739	N
ATOM	277	CE1	HIS	1094	24.777	33.440	8.406	1.00	41.24		C
ANISOU	277	CE1	HIS	1094	4025	5022	6623	-1290	-724	-2210	C
ATOM	278	NE2	HIS	1094	23.657	33.874	8.963	1.00	36.80		N
ANISOU	278	NE2	HIS	1094	4282	3613	6088	-1106	-647	-1597	N
ATOM	279	C	HIS	1094	20.434	31.716	6.513	1.00	13.89		C
ANISOU	279	C	HIS	1094	2051	1579	1647	141	-41	-81	C
ATOM	280	O	HIS	1094	20.329	31.492	5.314	1.00	16.32		O
ANISOU	280	O	HIS	1094	2862	1648	1691	-1	-332	-66	O
ATOM	281	N	GLY	1095	19.997	32.825	7.101	1.00	14.85		N
ANISOU	281	N	GLY	1095	2291	1495	1858	244	157	99	N
ATOM	282	CA	GLY	1095	19.413	33.873	6.281	1.00	14.77		C
ANISOU	282	CA	GLY	1095	2245	1364	2004	15	-181	3	C
ATOM	283	C	GLY	1095	19.863	35.240	6.763	1.00	14.17		C
ANISOU	283	C	GLY	1095	2094	1503	1785	-10	-477	35	C
ATOM	284	O	GLY	1095	20.500	35.396	7.795	1.00	13.82		O
ANISOU	284	O	GLY	1095	1817	1780	1656	136	-282	63	O
ATOM	285	N	THR	1096	19.482	36.228	5.960	1.00	14.93		N
ANISOU	285	N	THR	1096	2591	1370	1710	-68	-380	138	N
ATOM	286	CA	THR	1096	19.766	37.624	6.240	1.00	15.41		C
ANISOU	286	CA	THR	1096	2350	1508	1999	-159	-225	-80	C
ATOM	287	CB	THR	1096	20.907	38.156	5.328	1.00	18.97		C
ANISOU	287	CB	THR	1096	2355	2191	2661	-535	-170	193	C
ATOM	288	OG1	THR	1096	22.104	37.394	5.564	1.00	20.86		O
ANISOU	288	OG1	THR	1096	2422	2917	2587	-173	70	200	O
ATOM	289	CG2	THR	1096	21.261	39.576	5.649	1.00	23.05		C
ANISOU	289	CG2	THR	1096	3735	2186	2837	-866	239	222	C
ATOM	290	C	THR	1096	18.504	38.443	6.026	1.00	14.55		C
ANISOU	290	C	THR	1096	2581	1420	1528	-27	-196	113	C
ATOM	291	O	THR	1096	17.902	38.352	4.954	1.00	16.83		O
ANISOU	291	O	THR	1096	2925	1870	1601	17	-370	9	O
ATOM	292	N	LEU	1097	18.065	39.238	7.001	1.00	15.49		N
ANISOU	292	N	LEU	1097	2796	1239	1848	-158	-14	-42	N
ATOM	293	CA	LEU	1097	17.003	40.211	6.858	1.00	16.19		C
ANISOU	293	CA	LEU	1097	2515	1496	2142	-152	313	163	C
ATOM	294	CB	LEU	1097	16.170	40.409	8.135	1.00	17.06		C
ANISOU	294	CB	LEU	1097	2356	2357	1768	-397	26	-99	C
ATOM	295	CG	LEU	1097	15.241	39.210	8.381	1.00	17.74		C
ANISOU	295	CG	LEU	1097	2592	2281	1867	-267	-82	739	C
ATOM	296	CD1	LEU	1097	14.818	39.199	9.834	1.00	24.35		C
ANISOU	296	CD1	LEU	1097	3560	3494	2198	-69	591	801	C
ATOM	297	CD2	LEU	1097	14.067	39.291	7.418	1.00	20.72		C

Table 1 (continued)

ANISOU	297	CD2	LEU	1097	2478	2467	2928	-509	-497	274	C
ATOM	298	C	LEU	1097	17.646	41.542	6.466	1.00	15.26		C
ANISOU	298	C	LEU	1097	2304	1381	2112	-122	-179	174	C
ATOM	299	O	LEU	1097	18.637	41.938	7.063	1.00	17.75		O
ANISOU	299	O	LEU	1097	2907	1532	2304	-270	-591	41	O
ATOM	300	N	LEU	1098	17.091	42.205	5.464	1.00	17.52		N
ANISOU	300	N	LEU	1098	3184	1514	1959	-383	-511	201	N
ATOM	301	CA	LEU	1098	17.640	43.414	4.866	1.00	16.97		C
ANISOU	301	CA	LEU	1098	2749	1566	2133	-124	-49	258	C
ATOM	302	CB	LEU	1098	18.114	43.120	3.436	1.00	19.15		C
ANISOU	302	CB	LEU	1098	2742	2390	2146	64	-77	150	C
ATOM	303	CG	LEU	1098	18.607	44.302	2.601	1.00	21.77		C
ANISOU	303	CG	LEU	1098	4274	2339	1657	218	191	73	C
ATOM	304	CD1	LEU	1098	19.880	44.867	3.248	1.00	26.19		C
ANISOU	304	CD1	LEU	1098	3755	2516	3678	-437	514	515	C
ATOM	305	CD2	LEU	1098	18.897	43.992	1.133	1.00	30.96		C
ANISOU	305	CD2	LEU	1098	6253	3706	1805	2293	790	351	C
ATOM	306	C	LEU	1098	16.592	44.501	4.845	1.00	17.65		C
ANISOU	306	C	LEU	1098	2624	1546	2538	-144	-140	99	C
ATOM	307	O	LEU	1098	15.539	44.265	4.250	1.00	19.16		O
ANISOU	307	O	LEU	1098	3027	1715	2539	90	-429	-145	O
ATOM	308	N	ASP	1099	16.823	45.667	5.449	1.00	16.43		N
ANISOU	308	N	ASP	1099	2638	1647	1957	-231	131	160	N
ATOM	309	CA	ASP	1099	15.824	46.729	5.343	1.00	16.01		C
ANISOU	309	CA	ASP	1099	2561	1901	1620	11	267	-167	C
ATOM	310	CB	ASP	1099	15.683	47.494	6.660	1.00	22.02		C
ANISOU	310	CB	ASP	1099	4017	2355	1996	-345	470	-593	C
ATOM	311	CG	ASP	1099	16.716	48.503	7.068	1.00	23.16		C
ANISOU	311	CG	ASP	1099	4684	1960	2156	-577	670	-659	C
ATOM	312	OD1	ASP	1099	17.616	48.827	6.252	1.00	23.23		O
ANISOU	312	OD1	ASP	1099	4876	1831	2119	-581	598	-139	O
ATOM	313	OD2	ASP	1099	16.616	48.978	8.241	1.00	26.73		O1-
ANISOU	313	OD2	ASP	1099	5007	3114	2036	-744	428	-880	O1-
ATOM	314	C	ASP	1099	16.152	47.661	4.167	1.00	17.27		C
ANISOU	314	C	ASP	1099	2528	2086	1949	39	-5	213	C
ATOM	315	O	ASP	1099	17.156	47.528	3.454	1.00	16.53		O
ANISOU	315	O	ASP	1099	2985	1593	1704	43	220	187	O
ATOM	316	N	ASN	1100	15.288	48.643	3.906	1.00	20.88		N
ANISOU	316	N	ASN	1100	3575	1876	2484	527	532	114	N
ATOM	317	CA	ASN	1100	15.424	49.422	2.678	1.00	19.64		C
ANISOU	317	CA	ASN	1100	2972	2021	2468	30	-299	250	C
ATOM	318	CB	ASN	1100	14.156	50.244	2.400	1.00	23.92		C
ANISOU	318	CB	ASN	1100	3128	3246	2713	518	-438	205	C
ATOM	319	CG	ASN	1100	14.055	50.811	1.000	1.00	24.41		C
ANISOU	319	CG	ASN	1100	3968	2514	2792	1195	-80	198	C
ATOM	320	OD1	ASN	1100	14.243	50.122	-0.011	1.00	22.03		O
ANISOU	320	OD1	ASN	1100	3360	2202	2807	37	109	85	O
ATOM	321	ND2	ASN	1100	13.750	52.093	0.901	1.00	31.01		N
ANISOU	321	ND2	ASN	1100	5196	2646	3939	1704	1842	557	N
ATOM	322	C	ASN	1100	16.600	50.361	2.763	1.00	17.79		C
ANISOU	322	C	ASN	1100	2954	1691	2113	260	184	-398	C

Table 1 (continued)

ATOM	323	O	ASN	1100	17.017	50.903	1.742	1.00	20.12		O
ANISOU	323	O	ASN	1100	3289	1945	2411	-91	-65	68	O
ATOM	324	N	ASP	1101	17.114	50.526	3.976	1.00	20.09		N
ANISOU	324	N	ASP	1101	3400	1859	2374	80	-288	-246	N
ATOM	325	CA	ASP	1101	18.291	51.372	4.122	1.00	20.77		C
ANISOU	325	CA	ASP	1101	3646	1932	2316	-276	6	-255	C
ATOM	326	CB	ASP	1101	18.233	52.124	5.453	1.00	26.26		C
ANISOU	326	CB	ASP	1101	4661	2746	2572	-823	90	-695	C
ATOM	327	CG	ASP	1101	17.015	53.047	5.478	1.00	34.17		C
ANISOU	327	CG	ASP	1101	7156	2780	3045	832	395	-937	C
ATOM	328	OD1	ASP	1101	16.760	53.624	4.402	1.00	32.73		O
ANISOU	328	OD1	ASP	1101	6770	2635	3031	700	599	-824	O
ATOM	329	OD2	ASP	1101	16.330	53.193	6.518	1.00	30.97		O1-
ANISOU	329	OD2	ASP	1101	6291	2452	3025	553	199	-592	O1-
ATOM	330	C	ASP	1101	19.562	50.558	4.082	1.00	20.72		C
ANISOU	330	C	ASP	1101	3420	2302	2149	-357	-317	465	C
ATOM	331	O	ASP	1101	20.679	51.045	4.185	1.00	25.71		O
ANISOU	331	O	ASP	1101	3586	2977	3205	-501	-1050	658	O
ATOM	332	N	GLY	1102	19.460	49.231	3.932	1.00	21.33		N
ANISOU	332	N	GLY	1102	3335	2231	2540	117	-237	314	N
ATOM	333	CA	GLY	1102	20.598	48.352	3.817	1.00	22.38		C
ANISOU	333	CA	GLY	1102	3131	2950	2421	284	384	1278	C
ATOM	334	C	GLY	1102	21.044	47.769	5.141	1.00	24.59		C
ANISOU	334	C	GLY	1102	3891	2884	2567	197	22	1321	C
ATOM	335	O	GLY	1102	22.090	47.103	5.229	1.00	27.76		O
ANISOU	335	O	GLY	1102	3674	3376	3497	183	-565	1286	O
ATOM	336	N	LYS	1103	20.263	48.010	6.204	1.00	21.29		N
ANISOU	336	N	LYS	1103	4055	1997	2037	-852	-314	562	N
ATOM	337	CA	LYS	1103	20.766	47.379	7.463	1.00	23.81		C
ANISOU	337	CA	LYS	1103	5015	1938	2095	-994	-758	486	C
ATOM	338	CB	LYS	1103	20.174	48.115	8.638	1.00	29.64		C
ANISOU	338	CB	LYS	1103	6249	2897	2115	-1122	-540	16	C
ATOM	343	C	LYS	1103	20.420	45.916	7.444	1.00	23.84		C
ANISOU	343	C	LYS	1103	4449	1974	2636	-889	-1236	667	C
ATOM	344	O	LYS	1103	19.374	45.537	6.933	1.00	21.10		O
ANISOU	344	O	LYS	1103	4038	2074	1906	-692	-681	390	O
ATOM	345	N	LYS	1104	21.280	45.078	7.998	1.00	24.29		N
ANISOU	345	N	LYS	1104	4202	2066	2960	-786	-1089	626	N
ATOM	346	CA	LYS	1104	20.992	43.654	7.970	1.00	23.84		C
ANISOU	346	CA	LYS	1104	4493	2000	2564	-605	-962	507	C
ATOM	347	CB	LYS	1104	21.975	42.987	7.003	1.00	28.84		C
ANISOU	347	CB	LYS	1104	4843	2666	3450	-371	-432	347	C
ATOM	348	CG	LYS	1104	21.803	43.566	5.593	1.00	29.67		C
ANISOU	348	CG	LYS	1104	4346	3490	3439	-342	342	816	C
ATOM	349	CD	LYS	1104	22.788	42.910	4.622	1.00	33.82		C
ANISOU	349	CD	LYS	1104	4578	4403	3867	398	108	405	C
ATOM	350	CE	LYS	1104	24.212	43.385	4.884	1.00	37.41		C
ANISOU	350	CE	LYS	1104	4710	5159	4345	-320	1026	-293	C
ATOM	351	NZ	LYS	1104	25.065	43.442	3.676	1.00	40.31		N1+
ANISOU	351	NZ	LYS	1104	5578	5814	3924	-95	922	1260	N1+
ATOM	352	C	LYS	1104	21.111	42.977	9.317	1.00	24.33		C

Table 1 (continued)

ANISOU	352	C	LYS	1104	4239	2235	2771	-1171	-1438	695	C
ATOM	353	O	LYS	1104	21.886	43.413	10.174	1.00	24.94		O
ANISOU	353	O	LYS	1104	3928	2262	3287	-982	-1742	758	O
ATOM	354	N	ILE	1105	20.318	41.892	9.455	1.00	20.58		N
ANISOU	354	N	ILE	1105	3608	1487	2725	-505	-917	204	N
ATOM	355	CA	ILE	1105	20.590	41.049	10.626	1.00	22.02		C
ANISOU	355	CA	ILE	1105	4488	1711	2169	-684	-641	83	C
ATOM	356	CB	ILE	1105	19.620	41.231	11.780	1.00	25.56		C
ANISOU	356	CB	ILE	1105	4854	2160	2696	2	-339	-206	C
ATOM	357	CG2	ILE	1105	19.736	42.592	12.465	1.00	33.79		C
ANISOU	357	CG2	ILE	1105	6745	2782	3311	-825	246	-910	C
ATOM	358	CG1	ILE	1105	18.185	40.968	11.324	1.00	24.34		C
ANISOU	358	CG1	ILE	1105	4595	2304	2350	412	-239	-29	C
ATOM	359	CD1	ILE	1105	17.424	40.521	12.575	1.00	28.23		C
ANISOU	359	CD1	ILE	1105	5098	3402	2224	-443	-505	299	C
ATOM	360	C	ILE	1105	20.520	39.608	10.180	1.00	18.60		C
ANISOU	360	C	ILE	1105	3389	1597	2080	444	-677	206	C
ATOM	361	O	ILE	1105	19.781	39.242	9.248	1.00	19.32		O
ANISOU	361	O	ILE	1105	3491	1563	2286	-345	-939	249	O
ATOM	362	N	HIS	1106	21.319	38.779	10.867	1.00	18.20		N
ANISOU	362	N	HIS	1106	3056	2013	1846	-526	-671	189	N
ATOM	363	CA	HIS	1106	21.224	37.357	10.624	1.00	16.97		C
ANISOU	363	CA	HIS	1106	2576	1862	2010	-61	-336	229	C
ATOM	364	CB	HIS	1106	22.248	36.488	11.375	1.00	22.26		C
ANISOU	364	CB	HIS	1106	3188	2598	2671	43	-1259	258	C
ATOM	365	CG	HIS	1106	23.632	36.932	11.124	1.00	29.93		C
ANISOU	365	CG	HIS	1106	2773	5051	3547	248	-1011	-798	C
ATOM	366	CD2	HIS	1106	24.422	37.798	11.793	1.00	37.58		C
ANISOU	366	CD2	HIS	1106	3127	6178	4972	-1142	235	-1730	C
ATOM	367	ND1	HIS	1106	24.373	36.470	10.065	1.00	35.04		N
ANISOU	367	ND1	HIS	1106	3693	5182	4437	590	-337	-1019	N
ATOM	368	CE1	HIS	1106	25.575	37.032	10.081	1.00	36.29		C
ANISOU	368	CE1	HIS	1106	3932	5372	4486	220	251	-453	C
ATOM	369	NE2	HIS	1106	25.627	37.842	11.123	1.00	38.30		N
ANISOU	369	NE2	HIS	1106	3359	5806	5387	-502	637	-1207	N
ATOM	370	C	HIS	1106	19.901	36.797	11.107	1.00	15.47		C
ANISOU	370	C	HIS	1106	2905	1407	1566	96	89	349	C
ATOM	371	O	HIS	1106	19.306	37.353	12.007	1.00	20.63		O
ANISOU	371	O	HIS	1106	4193	1513	2134	-41	852	130	O
ATOM	372	N	CYS	1107	19.486	35.692	10.504	1.00	15.17		N
ANISOU	372	N	CYS	1107	2373	1579	1814	186	-242	221	N
ATOM	373	CA	CYS	1107	18.299	35.001	10.980	1.00	15.24		C
ANISOU	373	CA	CYS	1107	2596	1560	1633	157	55	315	C
ATOM	374	CB	CYS	1107	17.012	35.611	10.446	1.00	16.18		C
ANISOU	374	CB	CYS	1107	2338	1974	1834	255	418	504	C
ATOM	375	SG	CYS	1107	16.865	35.601	8.615	1.00	16.14		S
ANISOU	375	SG	CYS	1107	2271	1948	1913	199	-45	516	S
ATOM	376	C	CYS	1107	18.449	33.532	10.562	1.00	14.82		C
ANISOU	376	C	CYS	1107	2259	1745	1627	105	-99	24	C
ATOM	377	O	CYS	1107	19.413	33.158	9.894	1.00	14.60		O
ANISOU	377	O	CYS	1107	2318	1851	1380	253	-148	257	O

Table 1 (continued)

ATOM	378	N	ALA	1108	17.464	32.760	11.000	1.00	15.07		N
ANISOU	378	N	ALA	1108	2576	1492	1658	171	180	117	N
ATOM	379	CA	ALA	1108	17.348	31.367	10.614	1.00	13.52		C
ANISOU	379	CA	ALA	1108	2375	1529	1232	345	-16	-8	C
ATOM	380	CB	ALA	1108	17.367	30.505	11.862	1.00	15.06		C
ANISOU	380	CB	ALA	1108	2968	1369	1387	203	-304	15	C
ATOM	381	C	ALA	1108	16.080	31.163	9.833	1.00	14.94		C
ANISOU	381	C	ALA	1108	2349	1854	1474	399	-87	48	C
ATOM	382	O	ALA	1108	15.035	31.700	10.251	1.00	19.41		O
ANISOU	382	O	ALA	1108	2542	2949	1884	784	-238	-499	O
ATOM	383	N	VAL	1109	16.079	30.444	8.733	1.00	13.81		N
ANISOU	383	N	VAL	1109	2237	1499	1512	137	-187	54	N
ATOM	384	CA	VAL	1109	14.890	30.344	7.898	1.00	15.47		C
ANISOU	384	CA	VAL	1109	2539	1515	1824	26	-362	289	C
ATOM	385	CB	VAL	1109	15.149	30.928	6.496	1.00	16.40		C
ANISOU	385	CB	VAL	1109	2607	1990	1633	-407	-429	275	C
ATOM	386	CG1	VAL	1109	13.897	30.883	5.665	1.00	17.25		C
ANISOU	386	CG1	VAL	1109	2613	2194	1747	-300	-469	90	C
ATOM	387	CG2	VAL	1109	15.659	32.365	6.632	1.00	16.33		C
ANISOU	387	CG2	VAL	1109	2060	1845	2298	-188	-308	437	C
ATOM	388	C	VAL	1109	14.466	28.882	7.821	1.00	14.66		C
ANISOU	388	C	VAL	1109	2433	1474	1664	110	-324	105	C
ATOM	389	O	VAL	1109	15.240	28.088	7.286	1.00	16.65		O
ANISOU	389	O	VAL	1109	2852	1651	1823	131	23	-27	O
ATOM	390	N	LYS	1110	13.288	28.599	8.364	1.00	15.46		N
ANISOU	390	N	LYS	1110	2347	1547	1979	-13	-340	85	N
ATOM	391	CA	LYS	1110	12.808	27.208	8.327	1.00	17.72		C
ANISOU	391	CA	LYS	1110	2658	1549	2528	-150	-514	-123	C
ATOM	392	CB	LYS	1110	12.111	26.845	9.620	1.00	21.03		C
ANISOU	392	CB	LYS	1110	3139	1834	3018	-291	-312	612	C
ATOM	393	CG	LYS	1110	11.338	25.507	9.662	1.00	20.82		C
ANISOU	393	CG	LYS	1110	2720	1928	3261	-327	-778	339	C
ATOM	394	CD	LYS	1110	12.291	24.345	9.457	1.00	23.85		C
ANISOU	394	CD	LYS	1110	3221	1921	3921	-132	-876	133	C
ATOM	395	CE	LYS	1110	11.673	22.978	9.329	1.00	29.36		C
ANISOU	395	CE	LYS	1110	3758	2067	5329	-365	226	-274	C
ATOM	396	NZ	LYS	1110	10.456	22.736	10.084	1.00	29.17		N1+
ANISOU	396	NZ	LYS	1110	4720	1822	4541	-444	694	-151	N1+
ATOM	397	C	LYS	1110	11.879	27.063	7.134	1.00	20.76		C
ANISOU	397	C	LYS	1110	3013	1951	2922	221	-879	-555	C
ATOM	398	O	LYS	1110	10.856	27.780	7.110	1.00	20.82		O
ANISOU	398	O	LYS	1110	2678	2302	2931	101	-766	-630	O
ATOM	399	N	SER	1111	12.221	26.187	6.195	1.00	20.32		N
ANISOU	399	N	SER	1111	3454	1748	2518	338	-765	-228	N
ATOM	400	CA	SER	1111	11.364	25.888	5.045	1.00	23.57		C
ANISOU	400	CA	SER	1111	3806	2299	2849	315	-1075	-512	C
ATOM	401	CB	SER	1111	12.201	25.396	3.878	1.00	27.76		C
ANISOU	401	CB	SER	1111	3824	3662	3062	0	-1020	-1266	C
ATOM	402	OG	SER	1111	11.498	25.189	2.676	1.00	42.14		O
ANISOU	402	OG	SER	1111	5683	7063	3265	797	-1657	-1928	O
ATOM	403	C	SER	1111	10.340	24.845	5.439	1.00	24.98		C

Table 1 (continued)

ANISOU	403	C	SER	1111	3971	2663	2858	46	-1352	-279	C
ATOM	404	O	SER	1111	10.624	23.979	6.292	1.00	27.49		O
ANISOU	404	O	SER	1111	4330	2449	3667	-116	-1758	-69	O
ATOM	405	N	LEU	1112	9.162	24.891	4.853	1.00	25.97		N
ANISOU	405	N	LEU	1112	3459	2928	3481	453	-935	55	N
ATOM	406	CA	LEU	1112	8.099	23.958	5.140	1.00	26.54		C
ANISOU	406	CA	LEU	1112	3871	3329	2885	15	-1123	49	C
ATOM	407	CB	LEU	1112	6.778	24.566	5.617	1.00	28.64		C
ANISOU	407	CB	LEU	1112	4042	4028	2811	75	-416	702	C
ATOM	408	CG	LEU	1112	6.673	25.263	6.981	1.00	35.42		C
ANISOU	408	CG	LEU	1112	5411	5109	2938	445	61	411	C
ATOM	409	CD1	LEU	1112	5.275	25.868	7.146	1.00	42.56		C
ANISOU	409	CD1	LEU	1112	5747	6294	4129	885	889	276	C
ATOM	410	CD2	LEU	1112	6.982	24.340	8.152	1.00	35.29		C
ANISOU	410	CD2	LEU	1112	4756	5792	2859	-1573	-713	897	C
ATOM	411	C	LEU	1112	7.826	23.161	3.848	1.00	33.48		C
ANISOU	411	C	LEU	1112	4834	4490	3397	-320	-1158	-747	C
ATOM	412	O	LEU	1112	6.662	22.930	3.579	1.00	39.94		O
ANISOU	412	O	LEU	1112	5053	5312	4810	368	-2203	-1565	O
ATOM	1	N	VAL	1121	1.340	25.478	5.568	1.00	72.47		N
ANISOU	1	N	VAL	1121	5592	8899	13045	-1574	1973	1002	N
ATOM	2	CA	VAL	1121	0.038	24.833	5.597	1.00	61.07		C
ANISOU	2	CA	VAL	1121	4968	6693	11545	-487	1166	221	C
ATOM	3	CB	VAL	1121	0.069	23.454	6.300	1.00	67.25		C
ANISOU	3	CB	VAL	1121	5568	6327	13657	-237	1373	448	C
ATOM	4	CG1	VAL	1121	-1.353	22.969	6.508	1.00	55.98		C
ANISOU	4	CG1	VAL	1121	4761	1994	14516	-1430	-2727	-1648	C
ATOM	5	CG2	VAL	1121	0.871	22.431	5.512	1.00	85.79		C
ANISOU	5	CG2	VAL	1121	10094	7587	14915	1698	1696	-299	C
ATOM	6	C	VAL	1121	-1.002	25.674	6.330	1.00	49.24		C
ANISOU	6	C	VAL	1121	4242	6355	8112	-477	-1276	-419	C
ATOM	7	O	VAL	1121	-0.657	26.225	7.377	1.00	54.11		O
ANISOU	7	O	VAL	1121	5031	5585	9943	-2387	-2393	-733	O
ATOM	8	N	SER	1122	-2.208	25.733	5.764	1.00	43.40		N
ANISOU	8	N	SER	1122	4244	6060	6187	-1134	-864	553	N
ATOM	9	CA	SER	1122	-3.232	26.566	6.404	1.00	39.26		C
ANISOU	9	CA	SER	1122	3836	5398	5683	-1070	-1940	375	C
ATOM	10	CB	SER	1122	-4.525	26.528	5.577	1.00	43.90		C
ANISOU	10	CB	SER	1122	4667	5623	6391	-1026	-2749	721	C
ATOM	11	OG	SER	1122	-5.212	27.745	5.795	1.00	48.91		O
ANISOU	11	OG	SER	1122	5138	6421	7023	-227	-3402	115	O
ATOM	12	C	SER	1122	-3.479	26.141	7.848	1.00	35.32		C
ANISOU	12	C	SER	1122	3546	4298	5578	-1165	-1820	-44	C
ATOM	13	O	SER	1122	-3.483	26.972	8.760	1.00	34.40		O
ANISOU	13	O	SER	1122	3128	4035	5906	-685	-1858	-101	O
ATOM	14	N	GLN	1123	-3.682	24.845	8.117	1.00	36.12		N
ANISOU	14	N	GLN	1123	3588	4270	5865	-1432	-2053	-234	N
ATOM	15	CA	GLN	1123	-3.861	24.395	9.495	1.00	35.36		C
ANISOU	15	CA	GLN	1123	3438	3931	6067	-1313	-2133	51	C
ATOM	16	CB	GLN	1123	-4.369	22.959	9.615	1.00	39.93		C
ANISOU	16	CB	GLN	1123	4128	4338	6704	-2111	-2580	40	C

Table 1 (continued)

ATOM	17	CG	GLN	1123	-3.776	22.071	8.538	1.00	51.55		C
ANISOU	17	CG	GLN	1123	6432	4402	8751	-1059	-2502	-1038	C
ATOM	18	CD	GLN	1123	-3.183	20.773	9.058	1.00	62.86		C
ANISOU	18	CD	GLN	1123	8215	5518	10152	133	-2114	-54	C
ATOM	19	OE1	GLN	1123	-3.830	19.713	8.974	1.00	73.59		O
ANISOU	19	OE1	GLN	1123	10215	4943	12804	-98	-3418	1053	O
ATOM	20	NE2	GLN	1123	-1.965	20.857	9.599	1.00	65.98		N
ANISOU	20	NE2	GLN	1123	7443	7441	10184	150	-1368	2052	N
ATOM	21	C	GLN	1123	-2.538	24.494	10.264	1.00	32.25		C
ANISOU	21	C	GLN	1123	3233	3442	5579	-1228	-1763	-661	C
ATOM	22	O	GLN	1123	-2.545	24.850	11.437	1.00	31.57		O
ANISOU	22	O	GLN	1123	3776	2974	5244	-1094	-1562	-81	O
ATOM	23	N	PHE	1124	-1.410	24.182	9.627	1.00	32.94		N
ANISOU	23	N	PHE	1124	3591	2949	5975	-149	-2046	-1123	N
ATOM	24	CA	PHE	1124	-0.147	24.339	10.360	1.00	32.07		C
ANISOU	24	CA	PHE	1124	3378	2467	6340	-353	-2007	-607	C
ATOM	25	CB	PHE	1124	1.005	23.944	9.439	1.00	33.05		C
ANISOU	25	CB	PHE	1124	3549	3324	5684	-110	-2427	-1263	C
ATOM	26	CG	PHE	1124	2.347	23.846	10.151	1.00	29.57		C
ANISOU	26	CG	PHE	1124	3290	2972	4972	-582	-1941	-228	C
ATOM	27	CD1	PHE	1124	2.570	22.757	10.992	1.00	33.21		C
ANISOU	27	CD1	PHE	1124	4327	3300	4994	-836	-1991	99	C
ATOM	28	CD2	PHE	1124	3.322	24.800	9.976	1.00	27.33		C
ANISOU	28	CD2	PHE	1124	3152	3024	4207	-396	-1038	-544	C
ATOM	29	CE1	PHE	1124	3.774	22.653	11.643	1.00	33.03		C
ANISOU	29	CE1	PHE	1124	4111	2984	5456	-464	-1788	583	C
ATOM	30	CE2	PHE	1124	4.541	24.713	10.623	1.00	25.55		C
ANISOU	30	CE2	PHE	1124	2951	3074	3684	-675	-756	-444	C
ATOM	31	CZ	PHE	1124	4.760	23.623	11.462	1.00	31.68		C
ANISOU	31	CZ	PHE	1124	3734	3435	4868	-454	-1270	110	C
ATOM	32	C	PHE	1124	0.046	25.755	10.866	1.00	30.72		C
ANISOU	32	C	PHE	1124	4081	2478	5115	-267	-2101	-521	C
ATOM	33	O	PHE	1124	0.464	26.024	11.996	1.00	29.09		O
ANISOU	33	O	PHE	1124	3054	3316	4683	-796	-1561	-141	O
ATOM	34	N	LEU	1125	-0.274	26.708	9.968	1.00	29.88		N
ANISOU	34	N	LEU	1125	4302	2539	4511	-1310	-1801	-326	N
ATOM	35	CA	LEU	1125	-0.186	28.106	10.385	1.00	30.03		C
ANISOU	35	CA	LEU	1125	4964	2455	3992	-1151	-1550	39	C
ATOM	36	CB	LEU	1125	-0.424	29.022	9.166	1.00	34.53		C
ANISOU	36	CB	LEU	1125	5602	3163	4355	-956	-1921	447	C
ATOM	37	CG	LEU	1125	0.637	28.998	8.092	1.00	32.22		C
ANISOU	37	CG	LEU	1125	5087	3371	3785	-1554	-2444	708	C
ATOM	38	CD1	LEU	1125	0.217	29.913	6.947	1.00	38.65		C
ANISOU	38	CD1	LEU	1125	6495	4256	3933	-1442	-3149	909	C
ATOM	39	CD2	LEU	1125	1.987	29.426	8.639	1.00	34.23		C
ANISOU	39	CD2	LEU	1125	5157	2590	5258	-1091	-3031	603	C
ATOM	40	C	LEU	1125	-1.175	28.456	11.473	1.00	28.26		C
ANISOU	40	C	LEU	1125	4081	2268	4390	-948	-1854	58	C
ATOM	41	O	LEU	1125	-0.836	29.105	12.463	1.00	28.07		O
ANISOU	41	O	LEU	1125	4000	3035	3632	-1170	-1627	313	O
ATOM	42	N	THR	1126	-2.458	28.069	11.362	1.00	29.89		N

Table 1 (continued)

ANISOU	42	N	THR	1126	3787	2436	5134	-373	-2603	401	N
ATOM	43	CA	THR	1126	-3.243	28.600	12.518	1.00	40.40		C
ANISOU	43	CA	THR	1126	3953	5618	5780	-31	-1707	457	C
ATOM	44	CB	THR	1126	-4.746	28.680	12.170	1.00	45.32		C
ANISOU	44	CB	THR	1126	3928	7468	5824	-327	-1709	753	C
ATOM	45	OG1	THR	1126	-5.596	28.227	13.250	1.00	59.39		O
ANISOU	45	OG1	THR	1126	5038	11238	6290	-886	132	-1180	O
ATOM	46	CG2	THR	1126	-5.011	27.796	10.956	1.00	50.18		C
ANISOU	46	CG2	THR	1126	2655	10678	5735	-411	-874	-625	C
ATOM	47	C	THR	1126	-2.915	27.768	13.755	1.00	37.03		C
ANISOU	47	C	THR	1126	3372	5091	5608	-575	-1324	412	C
ATOM	48	O	THR	1126	-3.200	28.196	14.866	1.00	37.84		O
ANISOU	48	O	THR	1126	3645	4985	5748	-1285	-689	487	O
ATOM	49	N	GLU	1127	-2.309	26.605	13.577	1.00	34.12		N
ANISOU	49	N	GLU	1127	2797	4193	5974	-1567	-1491	396	N
ATOM	50	CA	GLU	1127	-1.744	25.774	14.629	1.00	38.13		C
ANISOU	50	CA	GLU	1127	3272	4634	6583	-1134	-1544	741	C
ATOM	51	CB	GLU	1127	-1.171	24.484	14.025	1.00	48.00		C
ANISOU	51	CB	GLU	1127	5125	4605	8509	-558	-2123	208	C
ATOM	56	C	GLU	1127	-0.633	26.471	15.391	1.00	36.99		C
ANISOU	56	C	GLU	1127	3557	5093	5407	-1331	-1479	1100	C
ATOM	57	O	GLU	1127	-0.502	26.448	16.628	1.00	48.39		O
ANISOU	57	O	GLU	1127	4063	9169	5153	-2634	-499	679	O
ATOM	58	N	GLY	1128	0.211	27.120	14.591	1.00	25.15		N
ANISOU	58	N	GLY	1128	2581	2498	4475	60	-1241	6	N
ATOM	59	CA	GLY	1128	1.465	27.602	15.152	1.00	22.65		C
ANISOU	59	CA	GLY	1128	2748	2081	3775	177	-1292	33	C
ATOM	60	C	GLY	1128	1.599	29.102	15.329	1.00	20.93		C
ANISOU	60	C	GLY	1128	2744	2096	3110	240	-994	145	C
ATOM	61	O	GLY	1128	2.546	29.575	15.961	1.00	19.89		O
ANISOU	61	O	GLY	1128	2496	2105	2956	143	-651	30	O
ATOM	62	N	ILE	1129	0.692	29.919	14.798	1.00	22.67		N
ANISOU	62	N	ILE	1129	3052	2102	3460	452	-1123	94	N
ATOM	63	CA	ILE	1129	0.820	31.368	14.858	1.00	20.75		C
ANISOU	63	CA	ILE	1129	3180	2117	2589	-72	-1156	634	C
ATOM	64	CB	ILE	1129	-0.243	32.007	13.898	1.00	19.51		C
ANISOU	64	CB	ILE	1129	2081	2274	3058	50	-591	714	C
ATOM	65	CG2	ILE	1129	-1.700	31.731	14.229	1.00	21.61		C
ANISOU	65	CG2	ILE	1129	2453	2437	3320	37	237	735	C
ATOM	66	CG1	ILE	1129	-0.018	33.529	13.747	1.00	19.42		C
ANISOU	66	CG1	ILE	1129	2164	2293	2922	37	-733	889	C
ATOM	67	CD1	ILE	1129	1.421	33.802	13.305	1.00	20.99		C
ANISOU	67	CD1	ILE	1129	2634	2162	3180	-110	192	72	C
ATOM	68	C	ILE	1129	0.730	31.878	16.279	1.00	20.07		C
ANISOU	68	C	ILE	1129	2615	2165	2845	81	-436	295	C
ATOM	69	O	ILE	1129	1.163	33.014	16.552	1.00	22.80		O
ANISOU	69	O	ILE	1129	3052	2177	3433	221	-878	63	O
ATOM	70	N	ILE	1130	0.222	31.086	17.202	1.00	21.50		N
ANISOU	70	N	ILE	1130	2186	2904	3080	292	-322	639	N
ATOM	71	CA	ILE	1130	0.184	31.498	18.608	1.00	21.81		C
ANISOU	71	CA	ILE	1130	2392	2901	2993	135	-365	890	C

Table 1 (continued)

ATOM	72	CB	ILE	1130	-0.387	30.340	19.450	1.00	23.97		C
ANISOU	72	CB	ILE	1130	2219	3242	3645	-147	-74	1068	C
ATOM	73	CG2	ILE	1130	0.528	29.133	19.520	1.00	32.46		C
ANISOU	73	CG2	ILE	1130	3977	3002	5356	310	-376	1457	C
ATOM	74	CG1	ILE	1130	-0.736	30.739	20.881	1.00	29.64		C
ANISOU	74	CG1	ILE	1130	3929	3684	3648	-1053	371	1093	C
ATOM	75	CD1	ILE	1130	-1.361	29.577	21.653	1.00	35.98		C
ANISOU	75	CD1	ILE	1130	5169	4705	3798	-2202	-388	1712	C
ATOM	76	C	ILE	1130	1.537	31.912	19.124	1.00	21.45		C
ANISOU	76	C	ILE	1130	2383	2827	2942	-159	18	462	C
ATOM	77	O	ILE	1130	1.701	32.732	20.041	1.00	20.97		O
ANISOU	77	O	ILE	1130	2412	2393	3164	75	131	476	O
ATOM	78	N	MET	1131	2.603	31.369	18.556	1.00	19.58		N
ANISOU	78	N	MET	1131	2341	2260	2839	-267	-295	196	N
ATOM	79	CA	MET	1131	3.939	31.724	19.004	1.00	18.04		C
ANISOU	79	CA	MET	1131	2364	1634	2855	-28	-487	-1	C
ATOM	80	CB	MET	1131	4.984	30.859	18.289	1.00	19.41		C
ANISOU	80	CB	MET	1131	2535	1882	2958	96	-471	-188	C
ATOM	81	CG	MET	1131	5.273	31.261	16.862	1.00	22.00		C
ANISOU	81	CG	MET	1131	2426	2954	2979	236	-368	-17	C
ATOM	82	SD	MET	1131	6.430	30.202	15.919	1.00	21.10		S
ANISOU	82	SD	MET	1131	3230	1778	3010	-57	39	266	S
ATOM	83	CE	MET	1131	7.801	30.100	17.020	1.00	22.86		C
ANISOU	83	CE	MET	1131	2535	1581	4569	194	-191	-319	C
ATOM	84	C	MET	1131	4.234	33.230	18.801	1.00	17.51		C
ANISOU	84	C	MET	1131	2547	1647	2459	-41	-323	50	C
ATOM	85	O	MET	1131	5.141	33.738	19.474	1.00	17.77		O
ANISOU	85	O	MET	1131	2017	1699	3036	72	-152	-252	O
ATOM	86	N	LYS	1132	3.504	33.922	17.927	1.00	17.69		N
ANISOU	86	N	LYS	1132	2663	1790	2267	-50	-147	120	N
ATOM	87	CA	LYS	1132	3.771	35.365	17.772	1.00	16.74		C
ANISOU	87	CA	LYS	1132	2007	1830	2525	18	-536	251	C
ATOM	88	CB	LYS	1132	2.994	35.937	16.571	1.00	20.03		C
ANISOU	88	CB	LYS	1132	2429	2341	2840	216	-779	416	C
ATOM	89	CG	LYS	1132	1.553	36.289	17.024	1.00	21.87		C
ANISOU	89	CG	LYS	1132	2372	2620	3316	365	-774	819	C
ATOM	90	CD	LYS	1132	0.782	36.818	15.823	1.00	25.78		C
ANISOU	90	CD	LYS	1132	3024	3290	3480	869	-1143	612	C
ATOM	91	CE	LYS	1132	-0.506	37.490	16.241	1.00	29.34		C
ANISOU	91	CE	LYS	1132	3071	4937	3140	1348	-1285	447	C
ATOM	92	NZ	LYS	1132	-0.308	38.628	17.160	1.00	36.92		N1+
ANISOU	92	NZ	LYS	1132	4640	4017	5370	1264	-100	-57	N1+
ATOM	93	C	LYS	1132	3.423	36.127	19.036	1.00	17.59		C
ANISOU	93	C	LYS	1132	2235	1641	2807	151	-584	126	C
ATOM	94	O	LYS	1132	3.919	37.245	19.237	1.00	20.41		O
ANISOU	94	O	LYS	1132	2989	1644	3124	49	-1083	155	O
ATOM	95	N	ASP	1133	2.588	35.567	19.908	1.00	17.71		N
ANISOU	95	N	ASP	1133	1687	2341	2701	114	-561	-250	N
ATOM	96	CA	ASP	1133	2.180	36.209	21.123	1.00	19.73		C
ANISOU	96	CA	ASP	1133	2170	2501	2824	611	-567	-233	C
ATOM	97	CB	ASP	1133	0.759	35.768	21.475	1.00	22.85		C

Table 1 (continued)

ANISOU	97	CB	ASP	1133	2009	3708	2966	875	-335	-123	C
ATOM	98	CG	ASP	1133	-0.299	36.124	20.466	1.00	25.69		C
ANISOU	98	CG	ASP	1133	2404	3583	3774	474	-1087	-337	C
ATOM	99	OD1	ASP	1133	-0.222	37.154	19.779	1.00	31.92		O
ANISOU	99	OD1	ASP	1133	4537	3878	3714	1791	-909	5	O
ATOM	100	OD2	ASP	1133	-1.258	35.354	20.333	1.00	37.84		O1-
ANISOU	100	OD2	ASP	1133	2583	6074	5721	-557	-862	-1513	O1-
ATOM	101	C	ASP	1133	3.057	35.874	22.327	1.00	19.57		C
ANISOU	101	C	ASP	1133	2285	2386	2766	726	-605	-446	C
ATOM	102	O	ASP	1133	2.814	36.321	23.462	1.00	23.20		O
ANISOU	102	O	ASP	1133	3363	2582	2869	730	-692	-724	O
ATOM	103	N	PHE	1134	4.084	35.058	22.104	1.00	15.45		N
ANISOU	103	N	PHE	1134	1547	1477	2846	-81	-326	130	N
ATOM	104	CA	PHE	1134	4.985	34.723	23.190	1.00	15.56		C
ANISOU	104	CA	PHE	1134	1599	1325	2989	-123	-474	-23	C
ATOM	105	CB	PHE	1134	5.407	33.251	23.135	1.00	17.33		C
ANISOU	105	CB	PHE	1134	2217	1187	3182	-231	-354	359	C
ATOM	106	CG	PHE	1134	4.268	32.244	23.266	1.00	15.66		C
ANISOU	106	CG	PHE	1134	2001	1279	2671	-132	-653	255	C
ATOM	107	CD1	PHE	1134	3.054	32.498	23.882	1.00	19.74		C
ANISOU	107	CD1	PHE	1134	2421	2117	2962	-711	-91	-374	C
ATOM	108	CD2	PHE	1134	4.434	30.969	22.743	1.00	17.42		C
ANISOU	108	CD2	PHE	1134	2393	1245	2981	-183	-859	203	C
ATOM	109	CE1	PHE	1134	2.034	31.562	23.980	1.00	17.15		C
ANISOU	109	CE1	PHE	1134	2683	1666	2167	-708	-213	-40	C
ATOM	110	CE2	PHE	1134	3.446	30.022	22.829	1.00	16.40		C
ANISOU	110	CE2	PHE	1134	2113	1416	2703	-190	-931	262	C
ATOM	111	CZ	PHE	1134	2.245	30.287	23.448	1.00	16.42		C
ANISOU	111	CZ	PHE	1134	2551	1545	2144	-66	-647	182	C
ATOM	112	C	PHE	1134	6.216	35.628	23.134	1.00	13.98		C
ANISOU	112	C	PHE	1134	1660	1277	2375	-176	-154	-183	C
ATOM	113	O	PHE	1134	6.825	35.747	22.062	1.00	17.67		O
ANISOU	113	O	PHE	1134	2131	2319	2263	-328	-109	-313	O
ATOM	114	N	SER	1135	6.552	36.243	24.262	1.00	12.93		N
ANISOU	114	N	SER	1135	1498	1285	2129	-57	-253	108	N
ATOM	115	CA	SER	1135	7.684	37.146	24.343	1.00	11.74		C
ANISOU	115	CA	SER	1135	1360	1055	2047	137	-332	-90	C
ATOM	116	CB	SER	1135	7.266	38.636	24.273	1.00	13.92		C
ANISOU	116	CB	SER	1135	1784	1136	2369	315	-380	281	C
ATOM	117	OG	SER	1135	6.582	38.923	23.097	1.00	18.16		O
ANISOU	117	OG	SER	1135	2313	1925	2662	293	-688	425	O
ATOM	118	C	SER	1135	8.378	36.876	25.651	1.00	11.79		C
ANISOU	118	C	SER	1135	1598	1029	1850	296	-230	8	C
ATOM	119	O	SER	1135	8.077	37.530	26.668	1.00	13.31		O
ANISOU	119	O	SER	1135	1956	1198	1906	461	-40	9	O
ATOM	120	N	HIS	1136	9.299	35.924	25.645	1.00	10.04		N
ANISOU	120	N	HIS	1136	1434	806	1577	38	-173	66	N
ATOM	121	CA	HIS	1136	10.042	35.588	26.861	1.00	9.82		C
ANISOU	121	CA	HIS	1136	1276	799	1655	12	-95	86	C
ATOM	122	CB	HIS	1136	9.376	34.424	27.591	1.00	9.93		C
ANISOU	122	CB	HIS	1136	1182	939	1654	-12	-2	221	C

Table 1 (continued)

ATOM	123	CG	HIS	1136	10.034	34.102	28.896	1.00	9.54		C
ANISOU	123	CG	HIS	1136	1092	976	1555	21	99	33	C
ATOM	124	CD2	HIS	1136	9.676	34.443	30.165	1.00	9.85		C
ANISOU	124	CD2	HIS	1136	1480	655	1607	78	147	-71	C
ATOM	125	ND1	HIS	1136	11.205	33.365	28.946	1.00	8.72		N
ANISOU	125	ND1	HIS	1136	1160	717	1435	18	74	61	N
ATOM	126	CE1	HIS	1136	11.519	33.280	30.224	1.00	9.37		C
ANISOU	126	CE1	HIS	1136	1322	860	1380	-22	133	67	C
ATOM	127	NE2	HIS	1136	10.616	33.917	30.998	1.00	10.35		N
ANISOU	127	NE2	HIS	1136	1412	957	1563	125	87	-90	N
ATOM	128	C	HIS	1136	11.482	35.288	26.468	1.00	9.66		C
ANISOU	128	C	HIS	1136	1255	952	1463	-181	-20	89	C
ATOM	129	O	HIS	1136	11.673	34.636	25.416	1.00	9.82		O
ANISOU	129	O	HIS	1136	1318	934	1481	-18	-65	-26	O
ATOM	130	N	PRO	1137	12.471	35.711	27.237	1.00	10.09		N
ANISOU	130	N	PRO	1137	1324	961	1548	-160	-91	-15	N
ATOM	131	CD	PRO	1137	12.370	36.474	28.512	1.00	11.92		C
ANISOU	131	CD	PRO	1137	1736	1171	1623	-102	-172	-116	C
ATOM	132	CA	PRO	1137	13.862	35.492	26.871	1.00	10.67		C
ANISOU	132	CA	PRO	1137	1256	962	1837	-276	-93	58	C
ATOM	133	CB	PRO	1137	14.694	36.051	28.062	1.00	12.67		C
ANISOU	133	CB	PRO	1137	1568	1245	2001	-371	-272	-102	C
ATOM	134	CG	PRO	1137	13.736	36.240	29.164	1.00	17.19		C
ANISOU	134	CG	PRO	1137	1670	3026	1836	-511	-324	-304	C
ATOM	135	C	PRO	1137	14.242	34.024	26.695	1.00	9.58		C
ANISOU	135	C	PRO	1137	1324	1011	1306	-111	-64	181	C
ATOM	136	O	PRO	1137	15.255	33.758	25.992	1.00	11.79		O
ANISOU	136	O	PRO	1137	1196	1328	1957	25	131	381	O
ATOM	137	N	ASN	1138	13.512	33.101	27.287	1.00	9.06		N
ANISOU	137	N	ASN	1138	1272	893	1277	-144	-119	138	N
ATOM	138	CA	ASN	1138	13.902	31.681	27.137	1.00	9.51		C
ANISOU	138	CA	ASN	1138	1304	876	1434	35	-437	152	C
ATOM	139	CB	ASN	1138	14.029	31.046	28.537	1.00	8.44		C
ANISOU	139	CB	ASN	1138	887	991	1329	18	-144	116	C
ATOM	140	CG	ASN	1138	15.059	31.798	29.353	1.00	8.48		C
ANISOU	140	CG	ASN	1138	1035	896	1291	50	-163	-12	C
ATOM	141	OD1	ASN	1138	14.733	32.372	30.392	1.00	10.22		O
ANISOU	141	OD1	ASN	1138	1271	1170	1442	-86	55	-126	O
ATOM	142	ND2	ASN	1138	16.322	31.761	28.876	1.00	9.05		N
ANISOU	142	ND2	ASN	1138	983	1039	1417	34	-101	77	N
ATOM	143	C	ASN	1138	12.930	30.923	26.246	1.00	8.10		C
ANISOU	143	C	ASN	1138	881	948	1247	13	-31	-4	C
ATOM	144	O	ASN	1138	12.849	29.690	26.333	1.00	8.68		O
ANISOU	144	O	ASN	1138	1021	976	1302	59	-87	-57	O
ATOM	145	N	VAL	1139	12.234	31.617	25.380	1.00	8.68		N
ANISOU	145	N	VAL	1139	1013	1074	1212	-114	-133	11	N
ATOM	146	CA	VAL	1139	11.317	31.040	24.393	1.00	7.91		C
ANISOU	146	CA	VAL	1139	897	993	1116	-72	0	-17	C
ATOM	147	CB	VAL	1139	9.856	31.349	24.768	1.00	9.51		C
ANISOU	147	CB	VAL	1139	880	1335	1398	-35	-24	108	C
ATOM	148	CG1	VAL	1139	8.882	30.831	23.691	1.00	9.96		C

Table 1 (continued)

ANISOU	148	CG1	VAL	1139	1074	1196	1513	-87	-229	157	C
ATOM	149	CG2	VAL	1139	9.533	30.782	26.149	1.00	9.84		C
ANISOU	149	CG2	VAL	1139	1032	1365	1340	-32	129	25	C
ATOM	150	C	VAL	1139	11.675	31.603	23.038	1.00	8.34		C
ANISOU	150	C	VAL	1139	1108	912	1149	-17	-36	23	C
ATOM	151	O	VAL	1139	11.768	32.833	22.884	1.00	9.75		O
ANISOU	151	O	VAL	1139	1403	892	1411	-35	28	59	O
ATOM	152	N	LEU	1140	11.889	30.732	22.038	1.00	8.67		N
ANISOU	152	N	LEU	1140	1182	1064	1048	36	-120	-20	N
ATOM	153	CA	LEU	1140	12.237	31.217	20.715	1.00	9.13		C
ANISOU	153	CA	LEU	1140	1333	1073	1062	146	-28	43	C
ATOM	154	CB	LEU	1140	12.512	30.000	19.814	1.00	10.25		C
ANISOU	154	CB	LEU	1140	1631	1054	1210	3	79	-81	C
ATOM	155	CG	LEU	1140	13.111	30.363	18.446	1.00	11.11		C
ANISOU	155	CG	LEU	1140	1562	1457	1202	14	103	-155	C
ATOM	156	CD1	LEU	1140	14.565	30.728	18.637	1.00	14.60		C
ANISOU	156	CD1	LEU	1140	1475	1896	2178	-99	247	-78	C
ATOM	157	CD2	LEU	1140	12.877	29.194	17.482	1.00	12.76		C
ANISOU	157	CD2	LEU	1140	2174	1544	1131	247	-172	-167	C
ATOM	158	C	LEU	1140	11.126	32.067	20.133	1.00	10.00		C
ANISOU	158	C	LEU	1140	1345	1259	1195	179	-59	138	C
ATOM	159	O	LEU	1140	9.951	31.694	20.100	1.00	12.73		O
ANISOU	159	O	LEU	1140	1376	1689	1773	88	-121	374	O
ATOM	160	N	SER	1141	11.484	33.260	19.643	1.00	10.90		N
ANISOU	160	N	SER	1141	1642	1190	1309	241	-76	132	N
ATOM	161	CA	SER	1141	10.447	34.120	19.039	1.00	13.26		C
ANISOU	161	CA	SER	1141	2361	1267	1410	528	-421	114	C
ATOM	162	CB	SER	1141	10.817	35.559	19.220	1.00	19.24		C
ANISOU	162	CB	SER	1141	3068	1328	2913	447	-1004	-104	C
ATOM	163	OG	SER	1141	12.016	35.843	18.584	1.00	33.36		O
ANISOU	163	OG	SER	1141	3664	2550	6463	-736	-133	736	O
ATOM	164	C	SER	1141	10.298	33.817	17.567	1.00	11.99		C
ANISOU	164	C	SER	1141	1499	1685	1372	30	-91	309	C
ATOM	165	O	SER	1141	11.122	33.170	16.930	1.00	13.68		O
ANISOU	165	O	SER	1141	1870	1697	1630	103	-77	-35	O
ATOM	166	N	LEU	1142	9.208	34.311	17.034	1.00	13.20		N
ANISOU	166	N	LEU	1142	1798	1629	1587	106	-393	257	N
ATOM	167	CA	LEU	1142	8.959	34.364	15.613	1.00	13.00		C
ANISOU	167	CA	LEU	1142	1751	1708	1482	19	-262	430	C
ATOM	168	CB	LEU	1142	7.467	34.101	15.343	1.00	14.74		C
ATOM	169	CG	LEU	1142	7.026	34.223	13.891	1.00	14.30		C
ANISOU	169	CG	LEU	1142	1728	2027	1678	-28	-345	-11	C
ATOM	170	CD1	LEU	1142	7.679	33.152	13.024	1.00	15.60		C
ANISOU	170	CD1	LEU	1142	2045	1582	2300	-219	-267	-234	C
ATOM	171	CD2	LEU	1142	5.505	34.132	13.787	1.00	17.38		C
ANISOU	171	CD2	LEU	1142	1703	2264	2636	65	-670	38	C
ATOM	172	C	LEU	1142	9.364	35.716	15.044	1.00	12.80		C
ANISOU	172	C	LEU	1142	1808	1398	1658	43	-280	166	C
ATOM	173	O	LEU	1142	8.843	36.726	15.533	1.00	14.64		O
ANISOU	173	O	LEU	1142	1903	1690	1969	281	-204	125	O
ATOM	174	N	LEU	1143	10.254	35.782	14.051	1.00	12.49		N

Table 1 (continued)

ANISOU	174	N	LEU	1143	1918	1334	1493	-21	-292	303	N
ATOM	175	CA	LEU	1143	10.535	37.074	13.436	1.00	12.91		C
ANISOU	175	CA	LEU	1143	1908	1206	1791	-28	-328	257	C
ATOM	176	CB	LEU	1143	11.922	37.108	12.786	1.00	14.81		C
ANISOU	176	CB	LEU	1143	1935	1567	2126	-57	-133	488	C
ATOM	177	CG	LEU	1143	13.059	36.879	13.779	1.00	16.06		C
ANISOU	177	CG	LEU	1143	1959	1832	2311	94	-247	147	C
ATOM	178	CD1	LEU	1143	14.428	37.113	13.126	1.00	16.05		C
ANISOU	178	CD1	LEU	1143	1970	1619	2508	-96	-256	355	C
ATOM	179	CD2	LEU	1143	12.893	37.771	14.994	1.00	23.19		C
ANISOU	179	CD2	LEU	1143	3172	3313	2326	-89	-85	-462	C
ATOM	180	C	LEU	1143	9.503	37.363	12.373	1.00	14.41		C
ANISOU	180	C	LEU	1143	2058	1382	2035	-63	-502	491	C
ATOM	181	O	LEU	1143	9.104	38.520	12.218	1.00	17.67		O
ANISOU	181	O	LEU	1143	2912	1655	2147	453	-717	292	O
ATOM	182	N	GLY	1144	9.050	36.383	11.613	1.00	14.23		N
ANISOU	182	N	GLY	1144	2053	1709	1645	-29	-436	362	N
ATOM	183	CA	GLY	1144	7.930	36.619	10.702	1.00	17.26		C
ANISOU	183	CA	GLY	1144	2812	1857	1889	472	-929	148	C
ATOM	184	C	GLY	1144	7.844	35.456	9.715	1.00	16.18		C
ANISOU	184	C	GLY	1144	2303	1670	2173	59	-867	196	C
ATOM	185	O	GLY	1144	8.522	34.433	9.864	1.00	15.88		O
ANISOU	185	O	GLY	1144	2444	1547	2044	38	-588	343	O
ATOM	186	N	ILE	1145	6.995	35.653	8.705	1.00	16.06		N
ANISOU	186	N	ILE	1145	1921	2244	1936	-3	-661	173	N
ATOM	187	CA	ILE	1145	6.720	34.638	7.698	1.00	15.81		C
ANISOU	187	CA	ILE	1145	2276	1985	1746	-42	-547	358	C
ATOM	188	CB	ILE	1145	5.312	34.045	7.892	1.00	20.34		C
ANISOU	188	CB	ILE	1145	2944	2930	1854	-1027	-298	154	C
ATOM	189	CG2	ILE	1145	4.940	32.994	6.861	1.00	23.35		C
ANISOU	189	CG2	ILE	1145	3106	3362	2403	-938	-356	-338	C
ATOM	190	CG1	ILE	1145	5.147	33.476	9.311	1.00	20.25		C
ANISOU	190	CG1	ILE	1145	2579	3064	2050	-570	-490	588	C
ATOM	191	CD1	ILE	1145	3.699	33.400	9.788	1.00	24.08		C
ANISOU	191	CD1	ILE	1145	3186	2686	3279	-834	533	535	C
ATOM	192	C	ILE	1145	6.834	35.200	6.279	1.00	16.04		C
ANISOU	192	C	ILE	1145	2383	1854	1857	-311	-530	397	C
ATOM	193	O	ILE	1145	6.263	36.254	6.005	1.00	19.29		O
ANISOU	193	O	ILE	1145	3771	1665	1893	-90	-630	394	O
ATOM	194	N	CYS	1146	7.544	34.512	5.419	1.00	17.58		N
ANISOU	194	N	CYS	1146	2340	2492	1847	-124	-369	467	N
ATOM	195	CA	CYS	1146	7.620	35.005	4.036	1.00	18.21		C
ANISOU	195	CA	CYS	1146	2687	2460	1772	304	-712	350	C
ATOM	196	CB	CYS	1146	9.073	35.113	3.618	1.00	21.06		C
ANISOU	196	CB	CYS	1146	3163	2514	2326	-294	190	365	C
ATOM	197	SG	CYS	1146	9.273	35.635	1.864	1.00	27.17		S
ANISOU	197	SG	CYS	1146	3967	3707	2651	324	97	935	S
ATOM	198	C	CYS	1146	6.768	34.057	3.206	1.00	20.26		C
ANISOU	198	C	CYS	1146	2772	2881	2044	296	-581	-36	C
ATOM	199	O	CYS	1146	7.037	32.847	3.101	1.00	21.86		O
ANISOU	199	O	CYS	1146	3105	2863	2337	65	-564	-208	O

Table 1 (continued)

ATOM	200	N	LEU	1147	5.722	34.608	2.603	1.00	25.84		N
ANISOU	200	N	LEU	1147	3324	3164	3329	-256	-1659	573	N
ATOM	201	CA	LEU	1147	4.730	33.851	1.836	1.00	30.79		C
ANISOU	201	CA	LEU	1147	3619	4302	3778	-789	-1616	-1	C
ATOM	202	CB	LEU	1147	3.320	34.416	2.066	1.00	33.11		C
ANISOU	202	CB	LEU	1147	3544	4697	4339	-498	-2144	281	C
ATOM	203	CG	LEU	1147	2.882	34.388	3.540	1.00	33.72		C
ANISOU	203	CG	LEU	1147	3081	4708	5023	-1047	-1079	565	C
ATOM	204	CD1	LEU	1147	1.502	34.986	3.730	1.00	45.99		C
ANISOU	204	CD1	LEU	1147	3244	8470	5761	110	-1226	1641	C
ATOM	205	CD2	LEU	1147	2.918	32.963	4.072	1.00	44.69		C
ANISOU	205	CD2	LEU	1147	5782	5089	6109	-1294	-1077	1276	C
ATOM	206	C	LEU	1147	5.070	33.862	0.359	1.00	39.93		C
ANISOU	206	C	LEU	1147	5100	6313	3757	-1526	-1509	-554	C
ATOM	207	O	LEU	1147	4.554	33.091	-0.466	1.00	47.45		O
ANISOU	207	O	LEU	1147	6055	7604	4369	-1710	-1748	-1357	O
ATOM	208	N	ARG	1148	5.981	34.747	-0.059	1.00	46.27		N
ANISOU	208	N	ARG	1148	6720	7485	3377	-2429	-1417	400	N
ATOM	209	CA	ARG	1148	6.602	34.494	-1.363	1.00	56.44		C
ANISOU	209	CA	ARG	1148	8079	8903	4463	-2251	-99	-10	C
ATOM	210	CB	ARG	1148	7.113	35.762	-2.013	1.00	57.07		C
ANISOU	210	CB	ARG	1148	9237	9419	3027	-2936	-268	-147	C
ATOM	211	C	ARG	1148	7.702	33.451	-1.129	1.00	69.14		C
ANISOU	211	C	ARG	1148	9984	10125	6161	-508	503	-86	C
ATOM	212	O	ARG	1148	7.644	32.849	-0.011	1.00	77.51		O
ANISOU	212	O	ARG	1148	9835	13187	6428	3652	2875	1106	O
ATOM	213	OXT	ARG	1148	8.578	33.240	-2.008	1.00	68.86		O1-
ANISOU	213	OXT	ARG	1148	11502	9299	5363	718	1004	1658	O1-
ATOM	1	N	PRO	1153	5.973	28.468	2.246	1.00	34.94		N
ANISOU	1	N	PRO	1153	4567	4013	4697	-1777	-2050	-152	N
ATOM	2	CD	PRO	1153	4.864	27.579	2.655	1.00	41.86		C
ANISOU	2	CD	PRO	1153	4433	5580	5895	-2041	-1191	-180	C
ATOM	3	CA	PRO	1153	6.143	29.558	3.217	1.00	36.18		C
ANISOU	3	CA	PRO	1153	4538	5364	3844	-1397	-2079	-548	C
ATOM	4	CB	PRO	1153	5.021	29.438	4.223	1.00	40.59		C
ANISOU	4	CB	PRO	1153	3893	7055	4475	-1319	-2157	-464	C
ATOM	5	CG	PRO	1153	4.143	28.343	3.725	1.00	45.43		C
ANISOU	5	CG	PRO	1153	4877	6509	5875	-1832	-1322	-630	C
ATOM	6	C	PRO	1153	7.491	29.345	3.908	1.00	28.05		C
ANISOU	6	C	PRO	1153	4166	3634	2857	-1103	-1285	-28	C
ATOM	7	O	PRO	1153	7.925	28.199	4.077	1.00	30.49		O
ANISOU	7	O	PRO	1153	4729	3156	3699	-1443	-802	-341	O
ATOM	8	N	LEU	1154	8.061	30.479	4.259	1.00	20.88		N
ANISOU	8	N	LEU	1154	2824	2973	2136	-184	-824	-56	N
ATOM	9	CA	LEU	1154	9.326	30.434	5.009	1.00	19.08		C
ANISOU	9	CA	LEU	1154	2664	2951	1636	-12	-538	-65	C
ATOM	10	CB	LEU	1154	10.435	31.205	4.303	1.00	19.26		C
ANISOU	10	CB	LEU	1154	2677	2742	1899	18	-225	-280	C
ATOM	11	CG	LEU	1154	10.818	30.672	2.924	1.00	21.16		C
ANISOU	11	CG	LEU	1154	3090	3024	1926	553	-137	-123	C
ATOM	12	CD1	LEU	1154	11.825	31.632	2.312	1.00	23.75		C

Table 1 (continued)

ANISOU	12	CD1	LEU	1154	3584	3487	1953	250	220	-195	C
ATOM	13	CD2	LEU	1154	11.341	29.227	3.004	1.00	22.18		C
ANISOU	13	CD2	LEU	1154	2823	3068	2535	634	-676	-500	C
ATOM	14	C	LEU	1154	9.074	30.989	6.401	1.00	17.48		C
ANISOU	14	C	LEU	1154	2736	2229	1677	218	-410	139	C
ATOM	15	O	LEU	1154	8.455	32.050	6.535	1.00	22.55		O
ANISOU	15	O	LEU	1154	3564	2757	2245	932	-667	65	O
ATOM	16	N	VAL	1155	9.536	30.307	7.432	1.00	17.71		N
ANISOU	16	N	VAL	1155	3125	1989	1613	54	-530	73	N
ATOM	17	CA	VAL	1155	9.355	30.724	8.810	1.00	15.48		C
ANISOU	17	CA	VAL	1155	2446	1774	1664	-136	-422	80	C
ATOM	18	CB	VAL	1155	8.958	29.541	9.706	1.00	15.52		C
ANISOU	18	CB	VAL	1155	2399	1717	1781	-38	-402	136	C
ATOM	19	CG1	VAL	1155	8.909	30.049	11.164	1.00	16.52		C
ANISOU	19	CG1	VAL	1155	2743	1823	1711	-33	-268	103	C
ATOM	20	CG2	VAL	1155	7.645	28.890	9.320	1.00	22.78		C
ANISOU	20	CG2	VAL	1155	3543	2117	2996	-1084	-557	-356	C
ATOM	21	C	VAL	1155	10.666	31.371	9.220	1.00	15.43		C
ANISOU	21	C	VAL	1155	2364	1757	1743	-122	-75	-99	C
ATOM	22	O	VAL	1155	11.711	30.709	9.235	1.00	18.49		O
ANISOU	22	O	VAL	1155	2407	1769	2851	-157	-467	172	O
ATOM	23	N	VAL	1156	10.651	32.656	9.547	1.00	15.66		N
ANISOU	23	N	VAL	1156	2505	1702	1742	-219	-296	23	N
ATOM	24	CA	VAL	1156	11.884	33.357	9.865	1.00	13.62		C
ANISOU	24	CA	VAL	1156	2240	1435	1500	89	-419	311	C
ATOM	25	CB	VAL	1156	11.903	34.745	9.184	1.00	15.37		C
ANISOU	25	CB	VAL	1156	2356	1699	1784	-88	-468	650	C
ATOM	26	CG1	VAL	1156	13.225	35.448	9.396	1.00	15.89		C
ANISOU	26	CG1	VAL	1156	2062	2105	1871	-149	85	445	C
ATOM	27	CG2	VAL	1156	11.596	34.594	7.681	1.00	16.61		C
ANISOU	27	CG2	VAL	1156	2475	2235	1602	292	-233	560	C
ATOM	28	C	VAL	1156	12.026	33.452	11.385	1.00	12.70		C
ANISOU	28	C	VAL	1156	1899	1440	1487	40	-207	304	C
ATOM	29	O	VAL	1156	11.123	33.958	12.052	1.00	12.84		O
ANISOU	29	O	VAL	1156	1724	1388	1768	-118	-252	42	O
ATOM	30	N	LEU	1157	13.172	32.954	11.869	1.00	12.85		N
ANISOU	30	N	LEU	1157	1910	1461	1509	95	-313	233	N
ATOM	31	CA	LEU	1157	13.436	32.801	13.289	1.00	12.63		C
ANISOU	31	CA	LEU	1157	1992	1162	1644	-46	-403	410	C
ATOM	32	CB	LEU	1157	13.516	31.299	13.647	1.00	12.41		C
ANISOU	32	CB	LEU	1157	1722	1055	1941	84	-129	225	C
ATOM	33	CG	LEU	1157	12.268	30.492	13.208	1.00	12.51		C
ANISOU	33	CG	LEU	1157	1720	1128	1904	58	-126	172	C
ATOM	34	CD1	LEU	1157	12.511	29.008	13.207	1.00	13.62		C
ANISOU	34	CD1	LEU	1157	2202	1119	1855	-17	-163	54	C
ATOM	35	CD2	LEU	1157	11.119	30.833	14.128	1.00	14.35		C
ANISOU	35	CD2	LEU	1157	1857	1272	2321	14	190	284	C
ATOM	36	C	LEU	1157	14.726	33.483	13.666	1.00	11.30		C
ANISOU	36	C	LEU	1157	1816	1005	1472	88	-59	-65	C
ATOM	37	O	LEU	1157	15.591	33.748	12.807	1.00	12.72		O
ANISOU	37	O	LEU	1157	1963	1305	1564	178	90	155	O

Table 1 (continued)

ATOM	38	N	PRO	1158	14.917	33.785	14.953	1.00	11.95		N
ANISOU	38	N	PRO	1158	1820	1283	1438	120	-117	91	N
ATOM	39	CD	PRO	1158	13.969	33.659	16.068	1.00	15.87		C
ANISOU	39	CD	PRO	1158	2092	2392	1546	-278	112	-318	C
ATOM	40	CA	PRO	1158	16.224	34.332	15.381	1.00	12.73		C
ANISOU	40	CA	PRO	1158	1756	1653	1430	203	-105	-177	C
ATOM	41	CB	PRO	1158	16.063	34.517	16.890	1.00	14.09		C
ANISOU	41	CB	PRO	1158	1998	1899	1458	223	-77	-288	C
ATOM	42	CG	PRO	1158	14.633	34.462	17.157	1.00	18.50		C
ANISOU	42	CG	PRO	1158	2273	2913	1843	-931	405	-660	C
ATOM	43	C	PRO	1158	17.366	33.366	15.098	1.00	11.34		C
ANISOU	43	C	PRO	1158	1711	1250	1345	-43	90	135	C
ATOM	44	O	PRO	1158	17.220	32.136	15.195	1.00	12.10		O
ANISOU	44	O	PRO	1158	1884	1177	1537	-105	63	213	O
ATOM	45	N	TYR	1159	18.502	33.964	14.747	1.00	11.59		N
ANISOU	45	N	TYR	1159	1682	1257	1466	-61	9	286	N
ATOM	46	CA	TYR	1159	19.734	33.223	14.588	1.00	11.92		C
ANISOU	46	CA	TYR	1159	1614	1324	1592	-82	12	340	C
ATOM	47	CB	TYR	1159	20.765	34.024	13.788	1.00	14.71		C
ANISOU	47	CB	TYR	1159	2023	1648	1917	22	383	704	C
ATOM	48	CG	TYR	1159	22.000	33.192	13.525	1.00	14.40		C
ANISOU	48	CG	TYR	1159	1930	1618	1922	-126	392	544	C
ATOM	49	CD1	TYR	1159	21.918	32.121	12.625	1.00	16.77		C
ANISOU	49	CD1	TYR	1159	2279	1981	2112	-142	587	238	C
ATOM	50	CE1	TYR	1159	23.050	31.339	12.372	1.00	19.27		C
ANISOU	50	CE1	TYR	1159	2504	2370	2450	-3	924	75	C
ATOM	51	CD2	TYR	1159	23.200	33.460	14.154	1.00	16.12		C
ANISOU	51	CD2	TYR	1159	1858	2234	2030	-168	429	461	C
ATOM	52	CE2	TYR	1159	24.322	32.688	13.903	1.00	18.57		C
ANISOU	52	CE2	TYR	1159	1780	3012	2264	-79	754	364	C
ATOM	53	CZ	TYR	1159	24.232	31.641	13.017	1.00	19.08		C
ANISOU	53	CZ	TYR	1159	2265	2712	2275	208	946	527	C
ATOM	54	OH	TYR	1159	25.371	30.872	12.776	1.00	25.18		O
ANISOU	54	OH	TYR	1159	2490	3626	3451	495	1329	209	O
ATOM	55	C	TYR	1159	20.310	32.885	15.961	1.00	11.18		C
ANISOU	55	C	TYR	1159	1564	1226	1457	-132	29	189	C
ATOM	56	O	TYR	1159	20.416	33.766	16.835	1.00	14.01		O
ANISOU	56	O	TYR	1159	2319	1255	1749	-305	36	37	O
ATOM	57	N	AMET	1160	20.661	31.631	16.167	0.50	11.05		N
ANISOU	57	N	AMET	1160	1505	1227	1466	-184	-191	154	N
ATOM	58	N	BMET	1160	20.662	31.621	16.088	0.50	10.59		N
ANISOU	58	N	BMET	1160	1504	1165	1354	-274	151	309	N
ATOM	59	CA	AMET	1160	21.137	31.112	17.455	0.50	11.05		C
ANISOU	59	CA	AMET	1160	1377	1378	1444	-252	42	334	C
ATOM	60	CA	BMET	1160	21.149	30.985	17.308	0.50	10.92		C
ANISOU	60	CA	BMET	1160	1472	1169	1509	-344	-52	265	C
ATOM	61	CB	AMET	1160	20.178	30.071	18.030	0.50	10.42		C
ANISOU	61	CB	AMET	1160	1296	1002	1663	-239	-6	80	C
ATOM	62	CB	BMET	1160	20.243	29.812	17.689	0.50	10.00		C
ANISOU	62	CB	BMET	1160	1379	986	1435	-219	7	279	C
ATOM	63	CG	AMET	1160	18.738	30.563	18.173	0.50	11.25		C

Table 1 (continued)

ANISOU	63	CG	AMET	1160	1267	1367	1640	-213	56	106	C
ATOM	64	CG	BMET	1160	18.822	30.248	18.059	0.50	9.96		C
ANISOU	64	CG	BMET	1160	1392	1044	1350	-125	-10	312	C
ATOM	65	SD	AMET	1160	18.509	31.858	19.425	0.50	12.21		S
ANISOU	65	SD	AMET	1160	1407	1589	1645	4	40	22	S
ATOM	66	SD	BMET	1160	18.767	31.013	19.708	0.50	10.37		S
ANISOU	66	SD	BMET	1160	1365	1141	1434	-125	-55	218	S
ATOM	67	CE	AMET	1160	18.488	30.897	20.925	0.50	14.21		C
ANISOU	67	CE	AMET	1160	2250	1461	1686	36	250	49	C
ATOM	68	CE	BMET	1160	18.006	32.605	19.307	0.50	11.82		C
ANISOU	68	CE	BMET	1160	1717	1316	1459	162	-144	129	C
ATOM	69	C	AMET	1160	22.534	30.577	17.202	0.50	10.25		C
ANISOU	69	C	AMET	1160	1388	1263	1245	-232	40	331	C
ATOM	70	C	BMET	1160	22.583	30.561	17.081	0.50	11.37		C
ANISOU	70	C	BMET	1160	1472	1298	1551	-311	101	321	C
ATOM	71	O	AMET	1160	22.707	29.436	16.752	0.50	11.53		O
ANISOU	71	O	AMET	1160	1688	1307	1386	-182	31	238	O
ATOM	72	O	BMET	1160	22.833	29.475	16.539	0.50	12.74		O
ANISOU	72	O	BMET	1160	1714	1477	1648	-283	266	111	O
ATOM	73	N	LYS	1161	23.533	31.411	17.482	1.00	12.71		N
ANISOU	73	N	LYS	1161	1418	1380	2031	-379	389	166	N
ATOM	74	CA	LYS	1161	24.930	31.154	17.093	1.00	14.68		C
ANISOU	74	CA	LYS	1161	1441	1604	2535	-322	498	227	C
ATOM	75	CB	LYS	1161	25.825	32.258	17.695	1.00	17.98		C
ANISOU	75	CB	LYS	1161	1617	1957	3256	-659	509	83	C
ATOM	76	CG	LYS	1161	27.322	32.073	17.511	1.00	23.11		C
ANISOU	76	CG	LYS	1161	1689	3236	3856	-1082	974	-407	C
ATOM	77	CD	LYS	1161	28.078	33.235	18.154	1.00	26.09		C
ANISOU	77	CD	LYS	1161	2294	3233	4387	-1786	608	239	C
ATOM	78	CE	LYS	1161	29.563	32.987	18.274	1.00	33.81		C
ANISOU	78	CE	LYS	1161	2423	4184	6239	-1770	-318	779	C
ATOM	79	NZ	LYS	1161	30.275	33.924	19.209	1.00	47.25		N1+
ANISOU	79	NZ	LYS	1161	2553	6700	8699	-1608	-615	-1584	N1+
ATOM	80	C	LYS	1161	25.450	29.797	17.500	1.00	14.28		C
ANISOU	80	C	LYS	1161	1466	1806	2154	-120	423	207	C
ATOM	81	O	LYS	1161	26.236	29.180	16.741	1.00	14.87		O
ANISOU	81	O	LYS	1161	1571	1960	2118	-69	370	162	O
ATOM	82	N	HIS	1162	25.070	29.285	18.674	1.00	12.76		N
ANISOU	82	N	HIS	1162	1296	1588	1965	-303	166	-19	N
ATOM	83	CA	HIS	1162	25.648	28.044	19.164	1.00	12.90		C
ANISOU	83	CA	HIS	1162	1220	1832	1848	-200	-92	50	C
ATOM	84	CB	HIS	1162	25.962	28.163	20.682	1.00	14.67		C
ANISOU	84	CB	HIS	1162	1073	2652	1849	-227	-91	-166	C
ATOM	85	CG	HIS	1162	27.043	29.176	20.880	1.00	16.06		C
ANISOU	85	CG	HIS	1162	1125	2543	2434	-163	-219	-385	C
ATOM	86	CD2	HIS	1162	27.067	30.393	21.432	1.00	19.23		C
ANISOU	86	CD2	HIS	1162	1722	3221	2365	-337	-316	-1044	C
ATOM	87	ND1	HIS	1162	28.333	28.909	20.414	1.00	18.56		N
ANISOU	87	ND1	HIS	1162	1033	2552	3467	-128	-199	-259	N
ATOM	88	CE1	HIS	1162	29.094	29.953	20.698	1.00	21.11		C
ANISOU	88	CE1	HIS	1162	1453	3128	3440	-580	-243	-339	C

Table 1 (continued)

ATOM	89	NE2	HIS	1162	28.373	30.873	21.317	1.00	22.12		N
ANISOU	89	NE2	HIS	1162	1972	3233	3200	-704	-458	-931	N
ATOM	90	C	HIS	1162	24.774	26.825	18.896	1.00	11.89		C
ANISOU	90	C	HIS	1162	1121	1648	1751	-189	25	252	C
ATOM	91	O	HIS	1162	25.092	25.750	19.399	1.00	14.32		O
ANISOU	91	O	HIS	1162	1257	1797	2388	8	68	460	O
ATOM	92	N	GLY	1163	23.701	27.010	18.121	1.00	10.70		N
ANISOU	92	N	GLY	1163	1060	1502	1503	-129	124	58	N
ATOM	93	CA	GLY	1163	22.905	25.849	17.704	1.00	10.95		C
ANISOU	93	CA	GLY	1163	1332	1383	1447	-200	108	157	C
ATOM	94	C	GLY	1163	22.146	25.221	18.855	1.00	9.41		C
ANISOU	94	C	GLY	1163	1123	1129	1323	-45	-29	69	C
ATOM	95	O	GLY	1163	21.821	25.844	19.866	1.00	10.12		O
ANISOU	95	O	GLY	1163	1212	1259	1375	-19	29	-80	O
ATOM	96	N	ASP	1164	21.855	23.917	18.669	1.00	9.68		N
ANISOU	96	N	ASP	1164	1259	1011	1407	133	-71	167	N
ATOM	97	CA	ASP	1164	20.992	23.250	19.652	1.00	9.15		C
ANISOU	97	CA	ASP	1164	1083	1168	1225	-136	-146	62	C
ATOM	98	CB	ASP	1164	20.319	21.986	19.073	1.00	10.27		C
ANISOU	98	CB	ASP	1164	1166	995	1741	85	-264	-56	C
ATOM	99	CG	ASP	1164	21.269	20.792	18.966	1.00	10.32		C
ANISOU	99	CG	ASP	1164	1268	1178	1476	218	11	154	C
ATOM	100	OD1	ASP	1164	21.970	20.638	17.934	1.00	13.19		O
ANISOU	100	OD1	ASP	1164	1717	1792	1502	408	60	-13	O
ATOM	101	OD2	ASP	1164	21.342	19.997	19.924	1.00	10.33		O1-
ANISOU	101	OD2	ASP	1164	1262	1139	1524	57	-272	162	O1-
ATOM	102	C	ASP	1164	21.805	22.949	20.920	1.00	8.82		C
ANISOU	102	C	ASP	1164	884	1106	1363	177	-116	148	C
ATOM	103	O	ASP	1164	23.008	22.721	20.904	1.00	9.29		O
ANISOU	103	O	ASP	1164	923	1108	1498	120	5	50	O
ATOM	104	N	LEU	1165	21.084	22.957	22.052	1.00	8.75		N
ANISOU	104	N	LEU	1165	1098	1030	1199	58	-77	17	N
ATOM	105	CA	LEU	1165	21.728	22.781	23.363	1.00	8.89		C
ANISOU	105	CA	LEU	1165	1025	1051	1300	120	-20	20	C
ATOM	106	CB	LEU	1165	20.617	22.986	24.418	1.00	9.14		C
ANISOU	106	CB	LEU	1165	883	1367	1225	5	-72	-115	C
ATOM	107	CG	LEU	1165	21.060	22.907	25.895	1.00	9.61		C
ANISOU	107	CG	LEU	1165	894	1481	1277	114	-116	-81	C
ATOM	108	CD1	LEU	1165	22.088	23.964	26.240	1.00	12.03		C
ANISOU	108	CD1	LEU	1165	1092	1704	1775	74	-451	-382	C
ATOM	109	CD2	LEU	1165	19.823	23.039	26.760	1.00	11.09		C
ANISOU	109	CD2	LEU	1165	1129	1788	1296	317	-1	-217	C
ATOM	110	C	LEU	1165	22.400	21.460	23.515	1.00	8.39		C
ANISOU	110	C	LEU	1165	805	954	1428	-71	12	185	C
ATOM	111	O	LEU	1165	23.451	21.383	24.165	1.00	9.20		O
ANISOU	111	O	LEU	1165	849	1243	1402	16	-22	3	O
ATOM	112	N	ARG	1166	21.845	20.378	22.945	1.00	8.83		N
ANISOU	112	N	ARG	1166	884	1003	1469	61	51	-25	N
ATOM	113	CA	ARG	1166	22.511	19.078	23.102	1.00	9.27		C
ANISOU	113	CA	ARG	1166	838	1032	1653	71	104	-33	C
ATOM	114	CB	ARG	1166	21.625	17.938	22.575	1.00	8.73		C

Table 1 (continued)

ANISOU	114	CB	ARG	1166	955	1020	1341	35	-76	-4	C
ATOM	115	CG	ARG	1166	22.229	16.601	22.998	1.00	10.57		C
ANISOU	115	CG	ARG	1166	1559	1031	1428	163	-345	-67	C
ATOM	116	CD	ARG	1166	21.594	15.428	22.256	1.00	10.93		C
ANISOU	116	CD	ARG	1166	1479	1015	1658	13	-208	-43	C
ATOM	117	NE	ARG	1166	22.235	14.192	22.683	1.00	10.73		N
ANISOU	117	NE	ARG	1166	1545	1013	1518	124	17	-6	N
ATOM	118	CZ	ARG	1166	22.522	13.160	21.904	1.00	10.46		C
ANISOU	118	CZ	ARG	1166	1331	1187	1458	109	-1	-54	C
ATOM	119	NH1	ARG	1166	22.242	13.138	20.597	1.00	12.64		N1+
ANISOU	119	NH1	ARG	1166	1796	1565	1442	344	-97	-74	N1+
ATOM	120	NH2	ARG	1166	23.110	12.113	22.493	1.00	11.73		N
ANISOU	120	NH2	ARG	1166	1497	1291	1667	378	-258	-154	N
ATOM	121	C	ARG	1166	23.857	19.056	22.395	1.00	8.56		C
ANISOU	121	C	ARG	1166	850	965	1439	128	14	102	C
ATOM	122	O	ARG	1166	24.874	18.672	22.971	1.00	9.40		O
ANISOU	122	O	ARG	1166	903	1166	1504	144	-49	66	O
ATOM	123	N	ASN	1167	23.889	19.474	21.116	1.00	9.82		N
ANISOU	123	N	ASN	1167	1065	1280	1385	37	38	48	N
ATOM	124	CA	ASN	1167	25.197	19.469	20.428	1.00	10.15		C
ANISOU	124	CA	ASN	1167	1038	1443	1376	-22	66	41	C
ATOM	125	CB	ASN	1167	25.028	19.756	18.952	1.00	12.52		C
ANISOU	125	CB	ASN	1167	1780	1677	1300	-39	81	47	C
ATOM	126	CG	ASN	1167	24.663	18.496	18.194	1.00	15.95		C
ANISOU	126	CG	ASN	1167	2272	1979	1809	391	-350	-454	C
ATOM	127	OD1	ASN	1167	25.311	17.444	18.360	1.00	19.03		O
ANISOU	127	OD1	ASN	1167	2346	2692	2193	-270	-527	-131	O
ATOM	128	ND2	ASN	1167	23.652	18.531	17.383	1.00	18.84		N
ANISOU	128	ND2	ASN	1167	3193	2002	1964	722	-108	-370	N
ATOM	129	C	ASN	1167	26.128	20.468	21.105	1.00	9.92		C
ANISOU	129	C	ASN	1167	1012	1251	1506	76	-71	134	C
ATOM	130	O	ASN	1167	27.344	20.222	21.086	1.00	10.86		O
ANISOU	130	O	ASN	1167	1007	1518	1603	56	76	116	O
ATOM	131	N	PHE	1168	25.640	21.552	21.688	1.00	9.56		N
ANISOU	131	N	PHE	1168	949	1363	1321	-7	-126	60	N
ATOM	132	CA	PHE	1168	26.523	22.491	22.353	1.00	9.90		C
ANISOU	132	CA	PHE	1168	1107	1206	1447	-39	-122	176	C
ATOM	133	CB	PHE	1168	25.751	23.738	22.820	1.00	10.48		C
ANISOU	133	CB	PHE	1168	1108	1169	1705	46	-105	124	C
ATOM	134	CG	PHE	1168	26.692	24.705	23.545	1.00	11.24		C
ANISOU	134	CG	PHE	1168	1305	1106	1858	37	-183	211	C
ATOM	135	CD1	PHE	1168	27.481	25.549	22.794	1.00	14.47		C
ANISOU	135	CD1	PHE	1168	1773	1238	2488	-358	226	42	C
ATOM	136	CD2	PHE	1168	26.774	24.756	24.953	1.00	11.95		C
ANISOU	136	CD2	PHE	1168	1300	1357	1884	260	-362	-80	C
ATOM	137	CE1	PHE	1168	28.340	26.413	23.454	1.00	17.10		C
ANISOU	137	CE1	PHE	1168	2233	1871	2392	-771	17	148	C
ATOM	138	CE2	PHE	1168	27.635	25.622	25.602	1.00	12.86		C
ANISOU	138	CE2	PHE	1168	1346	1497	2042	26	-342	92	C
ATOM	139	CZ	PHE	1168	28.416	26.462	24.827	1.00	17.13		C
ANISOU	139	CZ	PHE	1168	1938	2149	2422	-438	-180	287	C

Table 1 (continued)

ATOM	140	C	PHE	1168	27.228	21.840	23.532	1.00	9.35		C
ANISOU	140	C	PHE	1168	842	1194	1518	-134	-163	201	C
ATOM	141	O	PHE	1168	28.452	21.915	23.677	1.00	10.84		O
ANISOU	141	O	PHE	1168	833	1534	1751	-115	-55	159	O
ATOM	142	N	ILE	1169	26.460	21.157	24.415	1.00	9.26		N
ANISOU	142	N	ILE	1169	895	1178	1445	66	10	158	N
ATOM	143	CA	ILE	1169	27.087	20.594	25.606	1.00	9.31		C
ANISOU	143	CA	ILE	1169	1044	1226	1269	114	4	56	C
ATOM	144	CB	ILE	1169	26.058	20.237	26.671	1.00	8.97		C
ANISOU	144	CB	ILE	1169	918	1098	1391	81	-1	-18	C
ATOM	145	CG2	ILE	1169	25.344	21.514	27.158	1.00	10.44		C
ANISOU	145	CG2	ILE	1169	1252	1243	1470	311	-108	-186	C
ATOM	146	CG1	ILE	1169	25.073	19.144	26.241	1.00	9.61		C
ANISOU	146	CG1	ILE	1169	973	1192	1488	12	37	-55	C
ATOM	147	CD1	ILE	1169	23.942	18.876	27.210	1.00	9.89		C
ANISOU	147	CD1	ILE	1169	951	1125	1681	170	219	250	C
ATOM	148	C	ILE	1169	27.933	19.370	25.228	1.00	8.58		C
ANISOU	148	C	ILE	1169	876	1235	1151	64	36	125	C
ATOM	149	O	ILE	1169	28.808	18.986	26.005	1.00	9.69		O
ANISOU	149	O	ILE	1169	899	1301	1480	46	-152	83	O
ATOM	150	N	ARG	1170	27.722	18.752	24.067	1.00	9.58		N
ANISOU	150	N	ARG	1170	1083	1244	1311	205	-15	-23	N
ATOM	151	CA	ARG	1170	28.502	17.609	23.589	1.00	10.03		C
ANISOU	151	CA	ARG	1170	873	1465	1475	214	-2	-130	C
ATOM	152	CB	ARG	1170	27.745	16.759	22.556	1.00	10.30		C
ANISOU	152	CB	ARG	1170	1284	1118	1510	-31	6	11	C
ATOM	153	CG	ARG	1170	26.623	15.941	23.241	1.00	10.67		C
ANISOU	153	CG	ARG	1170	1187	1432	1434	34	7	166	C
ATOM	154	CD	ARG	1170	25.835	15.188	22.205	1.00	12.14		C
ANISOU	154	CD	ARG	1170	1121	1575	1917	-124	157	-198	C
ATOM	155	NE	ARG	1170	26.631	14.213	21.488	1.00	14.53		N
ANISOU	155	NE	ARG	1170	1576	1897	2048	23	273	-329	N
ATOM	156	CZ	ARG	1170	26.909	12.990	21.864	1.00	19.72		C
ANISOU	156	CZ	ARG	1170	2604	1954	2933	449	826	-136	C
ATOM	157	NH1	ARG	1170	26.476	12.462	23.017	1.00	22.85		N1+
ANISOU	157	NH1	ARG	1170	2993	2144	3544	101	1126	338	N1+
ATOM	158	NH2	ARG	1170	27.662	12.265	21.041	1.00	23.38		N
ANISOU	158	NH2	ARG	1170	3028	2152	3704	513	1139	-459	N
ATOM	159	C	ARG	1170	29.825	18.068	22.958	1.00	10.85		C
ANISOU	159	C	ARG	1170	881	1540	1699	201	34	-5	C
ATOM	160	O	ARG	1170	30.680	17.226	22.741	1.00	13.39		O
ANISOU	160	O	ARG	1170	1052	1676	2360	362	138	-254	O
ATOM	161	N	ASN	1171	29.985	19.353	22.645	1.00	10.72		N
ANISOU	161	N	ASN	1171	1041	1551	1480	77	-105	33	N
ATOM	162	CA	ASN	1171	31.201	19.813	22.000	1.00	11.35		C
ANISOU	162	CA	ASN	1171	992	1685	1636	120	-176	274	C
ATOM	163	CB	ASN	1171	30.911	21.192	21.364	1.00	13.78		C
ANISOU	163	CB	ASN	1171	1040	1973	2223	227	40	600	C
ATOM	164	CG	ASN	1171	32.049	21.700	20.502	1.00	15.68		C
ANISOU	164	CG	ASN	1171	1250	2415	2291	-271	-21	778	C
ATOM	165	OD1	ASN	1171	31.860	22.550	19.635	1.00	23.60		O

Table 1 (continued)

ANISOU	165	OD1	ASN	1171	2345	3350	3270	-269	-279	1759	O
ATOM	166	ND2	ASN	1171	33.242	21.224	20.675	1.00	13.78		N
ANISOU	166	ND2	ASN	1171	1210	2520	1506	-106	209	283	N
ATOM	167	C	ASN	1171	32.342	19.855	23.024	1.00	10.27		C
ANISOU	167	C	ASN	1171	1015	1336	1551	154	-77	22	C
ATOM	168	O	ASN	1171	32.387	20.776	23.831	1.00	11.56		O
ANISOU	168	O	ASN	1171	1266	1422	1702	202	-69	-109	O
ATOM	169	N	GLU	1172	33.239	18.896	22.898	1.00	10.88		N
ANISOU	169	N	GLU	1172	984	1672	1478	378	-170	-139	N
ATOM	170	CA	GLU	1172	34.254	18.810	23.960	1.00	11.57		C
ANISOU	170	CA	GLU	1172	1254	1313	1830	17	-538	185	C
ATOM	171	CB	GLU	1172	34.841	17.376	23.901	1.00	14.01		C
ANISOU	171	CB	GLU	1172	1720	1624	1981	554	-640	-132	C
ATOM	172	CG	GLU	1172	35.599	17.068	22.655	1.00	17.13		C
ANISOU	172	CG	GLU	1172	1913	1948	2648	276	155	136	C
ATOM	173	CD	GLU	1172	36.166	15.642	22.617	1.00	19.35		C
ANISOU	173	CD	GLU	1172	2582	2013	2759	554	429	-85	C
ATOM	174	OE1	GLU	1172	35.822	14.842	23.565	1.00	14.74		O1-
ANISOU	174	OE1	GLU	1172	1770	1720	2110	1	-510	-294	O1-
ATOM	175	OE2	GLU	1172	36.940	15.369	21.635	1.00	17.91		O
ANISOU	175	OE2	GLU	1172	1718	2706	2380	214	-208	-566	O
ATOM	176	C	GLU	1172	35.329	19.849	23.870	1.00	11.22		C
ANISOU	176	C	GLU	1172	1105	1618	1541	115	-148	12	C
ATOM	177	O	GLU	1172	36.157	19.948	24.778	1.00	13.09		O
ANISOU	177	O	GLU	1172	1204	1750	2021	-170	-412	215	O
ATOM	178	N	THR	1173	35.363	20.642	22.802	1.00	11.29		N
ANISOU	178	N	THR	1173	1170	1492	1629	132	73	-34	N
ATOM	179	CA	THR	1173	36.369	21.730	22.767	1.00	11.99		C
ANISOU	179	CA	THR	1173	1018	1784	1753	79	228	47	C
ATOM	180	CB	THR	1173	36.549	22.287	21.360	1.00	13.91		C
ANISOU	180	CB	THR	1173	1424	2064	1798	122	252	235	C
ATOM	181	OG1	THR	1173	35.346	22.942	20.917	1.00	17.61		O
ANISOU	181	OG1	THR	1173	1662	3107	1922	259	69	555	O
ATOM	182	CG2	THR	1173	36.861	21.132	20.402	1.00	17.96		C
ANISOU	182	CG2	THR	1173	2577	2554	1693	99	200	-31	C
ATOM	183	C	THR	1173	35.985	22.858	23.728	1.00	10.25		C
ANISOU	183	C	THR	1173	905	1313	1676	79	-94	286	C
ATOM	184	O	THR	1173	36.819	23.741	24.003	1.00	12.25		O
ANISOU	184	O	THR	1173	1111	1694	1850	-95	-282	310	O
ATOM	185	N	HIS	1174	34.752	22.852	24.227	1.00	9.98		N
ANISOU	185	N	HIS	1174	1056	1444	1291	147	87	243	N
ATOM	186	CA	HIS	1174	34.322	23.727	25.286	1.00	10.45		C
ANISOU	186	CA	HIS	1174	1170	1436	1363	33	0	165	C
ATOM	187	CB	HIS	1174	33.037	24.451	24.814	1.00	13.42		C
ANISOU	187	CB	HIS	1174	1528	1368	2201	426	-148	18	C
ATOM	188	CG	HIS	1174	32.414	25.395	25.810	1.00	14.01		C
ANISOU	188	CG	HIS	1174	1402	1626	2296	209	-59	-80	C
ATOM	189	CD2	HIS	1174	32.924	26.591	26.230	1.00	14.54		C
ANISOU	189	CD2	HIS	1174	1341	1694	2491	367	-355	-394	C
ATOM	190	ND1	HIS	1174	31.216	25.235	26.468	1.00	17.05		N
ANISOU	190	ND1	HIS	1174	1772	2329	2376	-29	199	-378	N

Table 1 (continued)

ATOM	191	CE1	HIS	1174	30.983	26.269	27.266	1.00	14.39		C
ANISOU	191	CE1	HIS	1174	1490	1995	1982	519	-282	-72	C
ATOM	192	NE2	HIS	1174	32.012	27.114	27.140	1.00	18.69		N
ANISOU	192	NE2	HIS	1174	1989	2098	3012	319	104	-499	N
ATOM	193	C	HIS	1174	34.064	22.915	26.536	1.00	9.30		C
ANISOU	193	C	HIS	1174	828	1307	1397	-172	181	49	C
ATOM	194	O	HIS	1174	33.655	21.746	26.424	1.00	11.98		O
ANISOU	194	O	HIS	1174	1520	1399	1632	-368	208	-137	O
ATOM	195	N	ASN	1175	34.272	23.492	27.713	1.00	8.83		N
ANISOU	195	N	ASN	1175	805	1194	1357	61	49	98	N
ATOM	196	CA	ASN	1175	33.947	22.790	28.969	1.00	9.09		C
ANISOU	196	CA	ASN	1175	845	1198	1409	151	71	208	C
ATOM	197	CB	ASN	1175	35.220	22.409	29.701	1.00	10.21		C
ANISOU	197	CB	ASN	1175	939	1224	1718	220	-30	333	C
ATOM	198	CG	ASN	1175	35.045	21.331	30.761	1.00	9.50		C
ANISOU	198	CG	ASN	1175	989	1125	1495	337	148	174	C
ATOM	199	OD1	ASN	1175	35.985	20.555	30.990	1.00	11.90		O
ANISOU	199	OD1	ASN	1175	1151	1415	1956	476	328	513	O
ATOM	200	ND2	ASN	1175	33.916	21.206	31.438	1.00	10.96		N
ANISOU	200	ND2	ASN	1175	1022	1293	1850	109	214	104	N
ATOM	201	C	ASN	1175	33.053	23.689	29.802	1.00	8.54		C
ANISOU	201	C	ASN	1175	856	916	1473	44	111	206	C
ATOM	202	O	ASN	1175	33.540	24.502	30.574	1.00	9.66		O
ANISOU	202	O	ASN	1175	838	1141	1693	100	-116	78	O
ATOM	203	N	PRO	1176	31.715	23.530	29.672	1.00	9.16		N
ANISOU	203	N	PRO	1176	874	1167	1437	43	57	-13	N
ATOM	204	CD	PRO	1176	30.974	22.648	28.762	1.00	11.31		C
ANISOU	204	CD	PRO	1176	944	1742	1611	46	-62	-255	C
ATOM	205	CA	PRO	1176	30.843	24.271	30.573	1.00	8.68		C
ANISOU	205	CA	PRO	1176	703	1197	1399	66	31	85	C
ATOM	206	CB	PRO	1176	29.432	23.796	30.212	1.00	12.91		C
ANISOU	206	CB	PRO	1176	836	2114	1956	-1	-76	-630	C
ATOM	207	CG	PRO	1176	29.579	23.200	28.839	1.00	13.63		C
ANISOU	207	CG	PRO	1176	851	2605	1725	58	14	-474	C
ATOM	208	C	PRO	1176	31.191	23.838	31.990	1.00	9.66		C
ANISOU	208	C	PRO	1176	929	1272	1469	268	122	153	C
ATOM	209	O	PRO	1176	31.615	22.709	32.207	1.00	10.84		O
ANISOU	209	O	PRO	1176	1145	1308	1664	255	142	336	O
ATOM	210	N	THR	1177	31.005	24.722	32.960	1.00	9.73		N
ANISOU	210	N	THR	1177	793	1434	1470	63	141	4	N
ATOM	211	CA	THR	1177	31.110	24.283	34.334	1.00	10.10		C
ANISOU	211	CA	THR	1177	955	1367	1514	-17	72	7	C
ATOM	212	CB	THR	1177	31.374	25.488	35.285	1.00	11.37		C
ANISOU	212	CB	THR	1177	764	1661	1893	-38	-119	-343	C
ATOM	213	OG1	THR	1177	30.261	26.381	35.119	1.00	11.62		O
ANISOU	213	OG1	THR	1177	932	1606	1879	34	-37	-384	O
ATOM	214	CG2	THR	1177	32.663	26.170	34.898	1.00	13.40		C
ANISOU	214	CG2	THR	1177	958	2076	2058	-342	-191	-64	C
ATOM	215	C	THR	1177	29.841	23.569	34.754	1.00	9.08		C
ANISOU	215	C	THR	1177	818	1246	1387	83	-51	15	C
ATOM	216	O	THR	1177	28.808	23.648	34.074	1.00	9.66		O

Table 1 (continued)

ANISOU	216	O	THR	1177	945	1360	1365	35	-83	-19	O
ATOM	217	N	VAL	1178	29.877	22.884	35.893	1.00	10.69		N
ANISOU	217	N	VAL	1178	1074	1578	1408	-8	-1	177	N
ATOM	218	CA	VAL	1178	28.653	22.333	36.451	1.00	9.95		C
ANISOU	218	CA	VAL	1178	1022	1513	1248	81	39	29	C
ATOM	219	CB	VAL	1178	28.903	21.572	37.778	1.00	12.30		C
ANISOU	219	CB	VAL	1178	1150	1902	1622	538	222	510	C
ATOM	220	CG1	VAL	1178	27.552	21.255	38.411	1.00	15.49		C
ANISOU	220	CG1	VAL	1178	1523	2066	2297	161	581	712	C
ATOM	221	CG2	VAL	1178	29.690	20.307	37.529	1.00	15.45		C
ANISOU	221	CG2	VAL	1178	1933	1708	2231	577	494	410	C
ATOM	222	C	VAL	1178	27.655	23.456	36.644	1.00	9.15		C
ANISOU	222	C	VAL	1178	998	1241	1238	-15	-223	45	C
ATOM	223	O	VAL	1178	26.471	23.277	36.334	1.00	9.57		O
ANISOU	223	O	VAL	1178	972	1407	1257	-87	-123	-51	O
ATOM	224	N	LYS	1179	28.078	24.598	37.142	1.00	9.80		N
ANISOU	224	N	LYS	1179	970	1477	1276	24	-201	-221	N
ATOM	225	CA	LYS	1179	27.194	25.741	37.336	1.00	10.25		C
ANISOU	225	CA	LYS	1179	1140	1482	1273	76	-262	-325	C
ATOM	226	CB	LYS	1179	27.997	26.923	37.906	1.00	11.45		C
ANISOU	226	CB	LYS	1179	1163	1477	1710	-67	-341	-265	C
ATOM	227	CG	LYS	1179	27.044	28.071	38.321	1.00	12.33		C
ANISOU	227	CG	LYS	1179	1238	1446	2002	-53	-295	-429	C
ATOM	228	CD	LYS	1179	27.909	29.254	38.803	1.00	16.72		C
ANISOU	228	CD	LYS	1179	1435	2073	2845	-233	-384	-1210	C
ATOM	229	CE	LYS	1179	27.041	30.445	39.212	1.00	17.61		C
ANISOU	229	CE	LYS	1179	2035	1848	2807	-438	502	-1052	C
ATOM	230	NZ	LYS	1179	26.482	30.163	40.568	1.00	16.98		N1+
ANISOU	230	NZ	LYS	1179	1332	1952	3167	-99	394	-155	N1+
ATOM	231	C	LYS	1179	26.524	26.135	36.024	1.00	9.59		C
ANISOU	231	C	LYS	1179	798	1492	1352	-25	-154	-122	C
ATOM	232	O	LYS	1179	25.322	26.379	35.975	1.00	9.69		O
ANISOU	232	O	LYS	1179	835	1330	1517	-10	-142	-223	O
ATOM	233	N	ASP	1180	27.312	26.198	34.953	1.00	9.18		N
ANISOU	233	N	ASP	1180	1041	1100	1346	-117	-82	-97	N
ATOM	234	CA	ASP	1180	26.762	26.551	33.653	1.00	8.85		C
ANISOU	234	CA	ASP	1180	942	979	1440	-185	-75	41	C
ATOM	235	CB	ASP	1180	27.812	26.499	32.547	1.00	9.53		C
ANISOU	235	CB	ASP	1180	813	1409	1401	-156	-95	30	C
ATOM	236	CG	ASP	1180	28.865	27.597	32.622	1.00	11.54		C
ANISOU	236	CG	ASP	1180	1045	1140	2200	-130	256	152	C
ATOM	237	OD1	ASP	1180	28.600	28.651	33.216	1.00	14.06		O
ANISOU	237	OD1	ASP	1180	1169	1307	2867	-285	368	-255	O
ATOM	238	OD2	ASP	1180	29.944	27.320	32.053	1.00	12.80		O1-
ANISOU	238	OD2	ASP	1180	1119	1429	2318	-208	474	162	O1-
ATOM	239	C	ASP	1180	25.667	25.584	33.216	1.00	8.59		C
ANISOU	239	C	ASP	1180	832	953	1477	-55	-122	-11	C
ATOM	240	O	ASP	1180	24.646	25.988	32.697	1.00	8.86		O
ANISOU	240	O	ASP	1180	803	1097	1466	79	-96	-134	O
ATOM	241	N	LEU	1181	25.912	24.282	33.426	1.00	8.71		N
ANISOU	241	N	LEU	1181	1044	883	1381	-65	-68	-116	N

Table 1 (continued)

ATOM	242	CA	LEU	1181	24.940	23.273	32.997	1.00	8.08		C
ANISOU	242	CA	LEU	1181	783	945	1342	-8	-56	-169	C
ATOM	243	CB	LEU	1181	25.539	21.872	33.168	1.00	8.70		C
ANISOU	243	CB	LEU	1181	823	890	1592	7	25	-133	C
ATOM	244	CG	LEU	1181	26.739	21.570	32.264	1.00	9.75		C
ANISOU	244	CG	LEU	1181	892	1322	1491	220	1	-157	C
ATOM	245	CD1	LEU	1181	27.383	20.260	32.714	1.00	11.15		C
ANISOU	245	CD1	LEU	1181	1049	1337	1852	366	-72	-289	C
ATOM	246	CD2	LEU	1181	26.353	21.502	30.791	1.00	10.62		C
ANISOU	246	CD2	LEU	1181	1169	1351	1514	-41	-35	-188	C
ATOM	247	C	LEU	1181	23.628	23.430	33.767	1.00	8.45		C
ANISOU	247	C	LEU	1181	886	1058	1266	109	-76	-117	C
ATOM	248	O	LEU	1181	22.519	23.364	33.215	1.00	8.81		O
ANISOU	248	O	LEU	1181	733	1196	1417	-5	-137	3	O
ATOM	249	N	ILE	1182	23.750	23.645	35.073	1.00	8.10		N
ANISOU	249	N	ILE	1182	859	1001	1219	45	-39	-36	N
ATOM	250	CA	ILE	1182	22.546	23.880	35.901	1.00	8.12		C
ANISOU	250	CA	ILE	1182	847	1007	1230	108	-2	29	C
ATOM	251	CB	ILE	1182	22.936	23.922	37.388	1.00	8.56		C
ANISOU	251	CB	ILE	1182	950	1092	1209	110	0	-121	C
ATOM	252	CG2	ILE	1182	21.709	24.249	38.242	1.00	9.90		C
ANISOU	252	CG2	ILE	1182	1131	1214	1417	140	182	-143	C
ATOM	253	CG1	ILE	1182	23.611	22.623	37.829	1.00	9.54		C
ANISOU	253	CG1	ILE	1182	968	1169	1488	82	-272	79	C
ATOM	254	CD1	ILE	1182	24.161	22.659	39.251	1.00	12.91		C
ANISOU	254	CD1	ILE	1182	1229	2447	1231	417	26	309	C
ATOM	255	C	ILE	1182	21.887	25.140	35.436	1.00	8.58		C
ANISOU	255	C	ILE	1182	841	942	1475	38	-125	-6	C
ATOM	256	O	ILE	1182	20.642	25.207	35.353	1.00	8.60		O
ANISOU	256	O	ILE	1182	857	1108	1301	80	-126	32	O
ATOM	257	N	GLY	1183	22.683	26.170	35.117	1.00	8.35		N
ANISOU	257	N	GLY	1183	1064	865	1245	-32	-93	-117	N
ATOM	258	CA	GLY	1183	22.101	27.428	34.635	1.00	8.61		C
ANISOU	258	CA	GLY	1183	1002	1045	1226	-167	-255	143	C
ATOM	259	C	GLY	1183	21.338	27.250	33.337	1.00	7.73		C
ANISOU	259	C	GLY	1183	817	906	1212	-181	-71	21	C
ATOM	260	O	GLY	1183	20.274	27.869	33.161	1.00	8.93		O
ANISOU	260	O	GLY	1183	886	1016	1492	32	-182	-50	O
ATOM	261	N	PHE	1184	21.826	26.416	32.414	1.00	8.29		N
ANISOU	261	N	PHE	1184	1041	807	1304	-96	-143	-55	N
ATOM	262	CA	PHE	1184	21.033	26.154	31.215	100	8.14		C
ANISOU	262	CA	PHE	1184	847	1033	1211	-87	-52	-25	C
ATOM	263	CB	PHE	1184	21.822	25.243	30.283	1.00	9.26		C
ANISOU	263	CB	PHE	1184	1013	1269	1235	-78	68	-104	C
ATOM	264	CG	PHE	1184	23.093	25.842	29.709	1.00	9.41		C
ANISOU	264	CG	PHE	1184	931	1277	1368	8	32	192	C
ATOM	265	CD1	PHE	1184	23.247	27.181	29.424	1.00	10.96		C
ANISOU	265	CD1	PHE	1184	995	1332	1837	-109	42	172	C
ATOM	266	CD2	PHE	1184	24.155	24.967	29.456	1.00	10.30		C
ANISOU	266	CD2	PHE	1184	901	1454	1558	9	64	92	C
ATOM	267	CE1	PHE	1184	24.444	27.650	28.871	1.00	12.83		C

Table 1 (continued)

ANISOU	267	CE1	PHE	1184	1173	1641	2060	-349	233	94	C
ATOM	268	CE2	PHE	1184	25.359	25.417	28.916	1.00	12.09		C
ANISOU	268	CE2	PHE	1184	875	1840	1880	-171	106	94	C
ATOM	269	CZ	PHE	1184	25.488	26.773	28.631	1.00	13.14		C
ANISOU	269	CZ	PHE	1184	1082	1833	2076	-319	215	30	C
ATOM	270	C	PHE	1184	19.703	25.510	31.559	1.00	7.61		C
ANISOU	270	C	PHE	1184	882	777	1233	-56	-70	-34	C
ATOM	271	O	PHE	1184	18.649	25.829	30.982	1.00	8.03		O
ANISOU	271	O	PHE	1184	822	966	1265	-8	-54	-14	O
ATOM	272	N	GLY	1185	19.703	24.613	32.540	1.00	7.78		N
ANISOU	272	N	GLY	1185	914	828	1215	-78	-9	-7	N
ATOM	273	CA	GLY	1185	18.469	23.994	32.979	1.00	7.93		C
ANISOU	273	CA	GLY	1185	757	889	1365	19	128	25	C
ATOM	274	C	GLY	1185	17.536	24.996	33.624	1.00	7.29		C
ANISOU	274	C	GLY	1185	763	721	1285	15	-148	53	C
ATOM	275	O	GLY	1185	16.299	24.956	33.419	1.00	8.20		O
ANISOU	275	O	GLY	1185	731	830	1554	0	-108	137	O
ATOM	276	N	LEU	1186	18.080	25.923	34.413	1.00	8.00		N
ANISOU	276	N	LEU	1186	1023	774	1244	-34	3	-6	N
ATOM	277	CA	LEU	1186	17.273	27.025	34.995	1.00	7.57		C
ANISOU	277	CA	LEU	1186	896	827	1153	11	-192	-46	C
ATOM	278	CB	LEU	1186	18.216	27.806	35.914	1.00	9.06		C
ANISOU	278	CB	LEU	1186	1064	1152	1226	73	-279	-261	C
ATOM	279	CG	LEU	1186	17.562	29.042	36.588	1.00	9.84		C
ANISOU	279	CG	LEU	1186	983	1292	1464	-178	40	-469	C
ATOM	280	CD1	LEU	1186	16.314	28.696	37.373	1.00	9.74		C
ANISOU	280	CD1	LEU	1186	994	1271	1437	-90	43	-44	C
ATOM	281	CD2	LEU	1186	18.613	29.718	37.467	1.00	10.69		C
ANISOU	281	CD2	LEU	1186	1084	1524	1454	-275	-196	-469	C
ATOM	282	C	LEU	1186	16.645	27.880	33.922	1.00	7.32		C
ANISOU	282	C	LEU	1186	828	757	1197	-98	-164	-40	C
ATOM	283	O	LEU	1186	15.465	28.227	34.010	1.00	7.86		O
ANISOU	283	O	LEU	1186	909	937	1139	38	-202	-42	O
ATOM	284	N	GLN	1187	17.424	28.211	32.884	1.00	7.78		N
ANISOU	284	N	GLN	1187	982	771	1205	-145	-128	56	N
ATOM	285	CA	GLN	1187	16.838	28.986	31.777	1.00	7.95		C
ANISOU	285	CA	GLN	1187	990	999	1030	-119	-148	-85	C
ATOM	286	CB	GLN	1187	17.926	29.326	30.729	1.00	8.51		C
ANISOU	286	CB	GLN	1187	1003	923	1308	-277	-20	-37	C
ATOM	287	CG	GLN	1187	18.991	30.293	31.300	1.00	9.79		C
ANISOU	287	CG	GLN	1187	1319	1045	1355	-421	-70	-152	C
ATOM	288	CD	GLN	1187	19.837	30.774	30.143	1.00	9.38		C
ANISOU	288	CD	GLN	1187	988	947	1630	-243	-101	17	C
ATOM	289	OE1	GLN	1187	19.281	31.298	29.162	1.00	10.71		O
ANISOU	289	OE1	GLN	1187	1365	1193	1513	-185	-54	120	O
ATOM	290	NE2	GLN	1187	21.140	30.613	30.212	1.00	12.77		N
ANISOU	290	NE2	GLN	1187	982	1468	2401	-85	-31	37	N
ATOM	291	C	GLN	1187	15.702	28.246	31.102	1.00	7.84		C
ANISOU	291	C	GLN	1187	788	852	1338	-71	-104	-31	C
ATOM	292	O	GLN	1187	14.664	28.831	30.786	1.00	8.11		O
ANISOU	292	O	GLN	1187	809	965	1307	36	-38	-124	O

Table 1 (continued)

ATOM	293	N	VAL	1188	15.871	26.936	30.837	1.00	7.53		N
ANISOU	293	N	VAL	1188	944	858	1058	-61	-108	-125	N
ATOM	294	CA	VAL	1188	14.741	26.164	30.246	1.00	8.06		C
ANISOU	294	CA	VAL	1188	926	944	1194	-69	-68	-231	C
ATOM	295	CB	VAL	1188	15.202	24.728	29.939	1.00	8.44		C
ANISOU	295	CB	VAL	1188	961	904	1341	-117	47	-232	C
ATOM	296	CG1	VAL	1188	13.999	23.891	29.493	1.00	8.98		C
ANISOU	296	CG1	VAL	1188	983	1003	1425	-90	-141	-263	C
ATOM	297	CG2	VAL	1188	16.288	24.736	28.871	1.00	9.31		C
ANISOU	297	CG2	VAL	1188	1087	1300	1150	32	51	-163	C
ATOM	298	C	VAL	1188	13.557	26.187	31.179	1.00	7.39		C
ANISOU	298	C	VAL	1188	855	750	1202	9	-148	-50	C
ATOM	299	O	VAL	1188	12.406	26.370	30.734	1.00	8.19		O
ANISOU	299	O	VAL	1188	848	805	1460	41	-249	-88	O
ATOM	300	N	ALA	1189	13.778	26.009	32.479	1.00	7.39		N
ANISOU	300	N	ALA	1189	857	797	1155	-12	-51	57	N
ATOM	301	CA	ALA	1189	12.653	26.049	33.421	1.00	8.04		C
ANISOU	301	CA	ALA	1189	930	923	1203	85	-41	53	C
ATOM	302	CB	ALA	1189	13.145	25.786	34.847	1.00	8.53		C
ANISOU	302	CB	ALA	1189	1201	912	1126	84	-134	-9	C
ATOM	303	C	ALA	1189	11.910	27.385	33.361	1.00	7.11		C
ANISOU	303	C	ALA	1189	769	924	1007	-32	-44	88	C
ATOM	304	O	ALA	1189	10.704	27.424	33.448	1.00	7.76		O
ANISOU	304	O	ALA	1189	804	958	1188	36	-66	-9	O
ATOM	305	N	LYS	1190	12.635	28.507	33.194	1.00	7.78		N
ANISOU	305	N	LYS	1190	963	842	1150	-32	-93	62	N
ATOM	306	CA	LYS	1190	11.978	29.807	33.121	1.00	8.03		C
ANISOU	306	CA	LYS	1190	983	864	1204	18	-186	-30	C
ATOM	307	CB	LYS	1190	13.021	30.920	33.178	1.00	8.26		C
ANISOU	307	CB	LYS	1190	966	851	1322	-21	-103	62	C
ATOM	308	CG	LYS	1190	13.672	31.051	34.569	1.00	9.20		C
ANISOU	308	CG	LYS	1190	1204	991	1301	-72	-197	-136	C
ATOM	309	CD	LYS	1190	14.763	32.108	34.640	1.00	11.45		C
ANISOU	309	CD	LYS	1190	1560	1198	1594	-254	-184	-203	C
ATOM	310	CE	LYS	1190	15.239	32.250	36.093	1.00	13.21		C
ANISOU	310	CE	LYS	1190	1812	1385	1820	-385	-572	-204	C
ATOM	311	NZ	LYS	1190	16.396	33.160	36.167	1.00	19.39		N1+
ANISOU	311	NZ	LYS	1190	2447	2201	2719	-1072	-709	-250	N1+
ATOM	312	C	LYS	1190	11.170	29.941	31.830	1.00	7.84		C
ANISOU	312	C	LYS	1190	916	865	1197	102	-104	-62	C
ATOM	313	O	LYS	1190	10.074	30.487	31.845	1.00	8.49		O
ANISOU	313	O	LYS	1190	865	884	1474	8	-81	143	O
ATOM	314	N	GLY	1191	11.700	29.438	30.715	1.00	7.81		N
ANISOU	314	N	GLY	1191	1125	725	1119	-101	-159	-52	N
ATOM	315	CA	GLY	1191	10.906	29.481	29.453	1.00	7.93		C
ANISOU	315	CA	GLY	1191	1000	917	1097	-247	-151	4	C
ATOM	316	C	GLY	1191	9.669	28.622	29.587	1.00	8.03		C
ANISOU	316	C	GLY	1191	877	728	1447	-74	-80	59	C
ATOM	317	O	GLY	1191	8.567	28.986	29.154	1.00	8.42		O
ANISOU	317	O	GLY	1191	964	875	1360	-27	-140	74	O
ATOM	318	N	MET	1192	9.798	27.435	30.207	1.00	8.56		N

Table 1 (continued)

ANISOU	318	N	MET	1192	874	774	1603	-35	-71	99	N
ATOM	319	CA	MET	1192	8.643	26.546	30.388	1.00	8.01		C
ANISOU	319	CA	MET	1192	915	711	1418	-95	5	6	C
ATOM	320	CB	MET	1192	9.120	25.161	30.827	1.00	881		C
ANISOU	320	CB	MET	1192	1100	715	1534	55	17	-40	C
ATOM	321	CG	MET	1192	9.884	24.386	29.740	1.00	9.44		C
ANISOU	321	CG	MET	1192	1020	1089	1479	95	-191	-307	C
ATOM	322	SD	MET	1192	8.997	24.234	28.167	1.00	9.74		S
ANISOU	322	SD	MET	1192	1286	1030	1386	-148	-77	32	S
ATOM	323	CE	MET	1192	7.489	23.426	28.713	1.00	12.16		C
ANISOU	323	CE	MET	1192	1287	1585	1748	-556	-126	-158	C
ATOM	324	C	MET	1192	7.686	27.121	31.412	1.00	7.76		C
ANISOU	324	C	MET	1192	848	761	1340	95	-143	95	C
ATOM	325	O	MET	1192	6.452	26.937	31.242	1.00	9.20		O
ANISOU	325	O	MET	1192	872	908	1714	54	-61	49	O
ATOM	326	N	LYS	1193	8.167	27.815	32.459	1.00	8.29		N
ANISOU	326	N	LYS	1193	1079	711	1360	106	-19	-24	N
ATOM	327	CA	LYS	1193	7.227	28.501	33.366	1.00	9.03		C
ANISOU	327	CA	LYS	1193	1115	981	1334	212	-79	11	C
ATOM	328	CB	LYS	1193	8.059	29.182	34.466	1.00	9.23		C
ANISOU	328	CB	LYS	1193	1232	892	1382	44	-119	-63	C
ATOM	329	CG	LYS	1193	7.250	30.053	35.443	1.00	11.20		C
ANISOU	329	CG	LYS	1193	1336	1316	1604	120	93	-211	C
ATOM	330	CD	LYS	1193	8.219	30.662	36.465	1.00	13.40		C
ANISOU	330	CD	LYS	1193	2106	1577	1407	39	-89	-262	C
ATOM	331	CE	LYS	1193	7.746	31.796	37.323	1.00	20.83		C
ANISOU	331	CE	LYS	1193	3758	1953	2204	313	-271	-873	C
ATOM	332	NZ	LYS	1193	8.837	32.282	38.290	1.00	18.80		N1+
ANISOU	332	NZ	LYS	1193	3621	1556	1967	-374	209	-563	N1+
ATOM	333	C	LYS	1193	6.380	29.472	32.596	1.00	8.41		C
ANISOU	333	C	LYS	1193	871	948	1378	114	25	21	C
ATOM	334	O	LYS	1193	5.163	29.588	32.794	1.00	10.02		O
ANISOU	334	O	LYS	1193	928	982	1897	162	23	55	O
ATOM	335	N	TYR	1194	6.996	30.230	31.675	1.00	8.89		N
ANISOU	335	N	TYR	1194	1192	739	1446	88	-87	17	N
ATOM	336	CA	TYR	1194	6.232	31.172	30.853	1.00	9.37		C
ANISOU	336	CA	TYR	1194	1118	987	1457	-86	-182	150	C
ATOM	337	CB	TYR	1194	7.203	31.994	30.038	1.00	9.58		C
ANISOU	337	CB	TYR	1194	1071	913	1657	-105	-122	170	C
ATOM	338	CG	TYR	1194	6.528	32.970	29.073	1.00	10.84		C
ANISOU	338	CG	TYR	1194	1244	1040	1835	2	-35	354	C
ATOM	339	CD1	TYR	1194	6.197	34.242	29.576	1.00	12.01		C
ANISOU	339	CD1	TYR	1194	1464	1044	2055	144	101	382	C
ATOM	340	CE1	TYR	1194	5.576	35.181	28.722	1.00	13.41		C
ANISOU	340	CE1	TYR	1194	1614	1143	2339	146	130	585	C
ATOM	341	CD2	TYR	1194	6.256	32.639	27.749	1.00	11.11		C
ANISOU	341	CD2	TYR	1194	1251	1227	1745	-204	-95	459	C
ATOM	342	CE2	TYR	1194	5.647	33.568	26.909	1.00	12.83		C
ANISOU	342	CE2	TYR	1194	1303	1639	1930	57	-94	548	C
ATOM	343	CZ	TYR	1194	5.314	34.821	27.410	1.00	14.24		C
ANISOU	343	CZ	TYR	1194	1283	1648	2481	303	-364	515	C

Table 1 (continued)

ATOM	344	OH	TYR	1194	4.730	35.731	26.592	1.00	16.96		O
ANISOU	344	OH	TYR	1194	1616	2189	2640	650	59	995	O
ATOM	345	C	TYR	1194	5.235	30.436	29.977	1.00	8.98		C
ANISOU	345	C	TYR	1194	908	868	1636	-74	-59	67	C
ATOM	346	O	TYR	1194	4.049	30.785	29.944	1.00	10.09		O
ANISOU	346	O	TYR	1194	912	896	2025	69	-188	77	O
ATOM	347	N	LEU	1195	5.679	29.407	29.260	1.00	9.32		N
ANISOU	347	N	LEU	1195	1026	862	1654	-53	-113	73	N
ATOM	348	CA	LEU	1195	4.723	28.673	28.384	1.00	9.50		C
ANISOU	348	CA	LEU	1195	1029	905	1675	-143	-88	23	C
ATOM	349	CB	LEU	1195	5.488	27.594	27.598	1.00	9.69		C
ANISOU	349	CB	LEU	1195	1043	1047	1593	51	-85	66	C
ATOM	350	CG	LEU	1195	6.436	28.134	26.519	1.00	11.10		C
ANISOU	350	CG	LEU	1195	981	1490	1747	-21	-60	219	C
ATOM	351	CD1	LEU	1195	7.197	26.966	25.904	1.00	12.70		C
ANISOU	351	CD1	LEU	1195	1421	1917	1486	263	34	159	C
ATOM	352	CD2	LEU	1195	5.714	28.961	25.433	1.00	12.45		C
ANISOU	352	CD2	LEU	1195	1421	1546	1763	-159	-347	311	C
ATOM	353	C	LEU	1195	3.586	28.075	29.162	1.00	8.80		C
ANISOU	353	C	LEU	1195	812	876	1656	87	-178	163	C
ATOM	354	O	LEU	1195	2.438	28.124	28.757	1.00	9.90		O
ANISOU	354	O	LEU	1195	837	1114	1811	124	-250	99	O
ATOM	355	N	ALA	1196	3.873	27.490	30.317	1.00	10.24		N
ANISOU	355	N	ALA	1196	1012	1218	1660	-81	-241	287	N
ATOM	356	CA	ALA	1196	2.825	26.895	31.150	1.00	10.58		C
ANISOU	356	CA	ALA	1196	1186	1223	1612	-50	-99	256	C
ATOM	357	CB	ALA	1196	3.452	26.131	32.305	1.00	11.69		C
ANISOU	357	CB	ALA	1196	1232	1381	1829	-203	-238	473	C
ATOM	358	C	ALA	1196	1.880	27.977	31.620	1.00	11.27		C
ANISOU	358	C	ALA	1196	1150	1330	1802	-23	-61	215	C
ATOM	359	O	ALA	1196	0.673	27.725	31.766	1.00	12.21		O
ANISOU	359	O	ALA	1196	1068	1682	1889	-82	-258	437	O
ATOM	360	N	SER	1197	2.365	29.198	31.882	1.00	11.07		N
ANISOU	360	N	SER	1197	1230	1251	1725	30	-131	169	N
ATOM	361	CA	SER	1197	1.512	30.299	32.338	1.00	13.17		C
ANISOU	361	CA	SER	1197	1514	1472	2017	260	-315	65	C
ATOM	362	CB	SER	1197	2.342	31.484	32.823	1.00	13.50		C
ANISOU	362	CB	SER	1197	1466	1673	1990	130	-71	-388	C
ATOM	363	OG	SER	1197	2.824	32.310	31.732	1.00	14.87		O
ANISOU	363	OG	SER	1197	1644	1832	2175	-136	-14	-369	O
ATOM	364	C	SER	1197	0.559	30.710	31.206	1.00	12.00		C
ANISOU	364	C	SER	1197	939	1600	2022	74	-115	102	C
ATOM	365	O	SER	1197	-0.521	31.234	31.500	1.00	14.85		O
ANISOU	365	O	SER	1197	1100	2130	2412	279	-110	-81	O
ATOM	366	N	LYS	1198	0.945	30.476	29.969	1.00	10.88		N
ANISOU	366	N	LYS	1198	1132	1026	1974	-63	-141	175	N
ATOM	367	CA	LYS	1198	0.100	30.685	28.800	1.00	11.12		C
ANISOU	367	CA	LYS	1198	1275	1010	1941	-42	-142	149	C
ATOM	368	CB	LYS	1198	0.980	31.129	27.631	1.00	12.15		C
ANISOU	368	CB	LYS	1198	1335	1235	2045	-280	-202	391	C
ATOM	369	CG	LYS	1198	1.783	32.383	27.855	1.00	13.20		C

Table 1 (continued)

ANISOU	369	CG	LYS	1198	1313	1282	2419	-276	-211	183	C
ATOM	370	CD	LYS	1198	0.944	33.589	28.193	1.00	19.28		C
ANISOU	370	CD	LYS	1198	1770	1267	4287	-30	-347	127	C
ATOM	371	CE	LYS	1198	1.883	34.780	28.433	1.00	26.75		C
ANISOU	371	CE	LYS	1198	2458	1398	6306	-254	-51	-598	C
ATOM	372	NZ	LYS	1198	1.049	35.986	28.782	1.00	35.73		N1+
ANISOU	372	NZ	LYS	1198	3366	1490	8720	-45	568	-920	N1+
ATOM	373	C	LYS	1198	-0.702	29.435	28.453	1.00	10.31		C
ANISOU	373	C	LYS	1198	1138	1057	1724	-10	-108	192	C
ATOM	374	O	LYS	1198	-1.386	29.475	27.418	1.00	11.86		O
ANISOU	374	O	LYS	1198	1175	1284	2047	-26	-368	291	O
ATOM	375	N	LYS	1199	-0.623	28.403	29.273	1.00	9.86		N
ANISOU	375	N	LYS	1199	980	1060	1706	-87	-22	220	N
ATOM	376	CA	LYS	1199	-1.400	27.161	29.120	1.00	9.82		C
ANISOU	376	CA	LYS	1199	860	1069	1802	-36	-69	58	C
ATOM	377	CB	LYS	1199	-2.908	27.423	29.220	1.00	11.06		C
ANISOU	377	CB	LYS	1199	872	1665	1664	-212	-4	189	C
ATOM	378	CG	LYS	1199	-3.217	28.025	30.584	1.00	13.03		C
ANISOU	378	CG	LYS	1199	1111	1697	2144	-188	203	-240	C
ATOM	379	CD	LYS	1199	-4.691	28.361	30.724	1.00	13.57		C
ANISOU	379	CD	LYS	1199	989	1796	2371	-330	290	-38	C
ATOM	380	CE	LYS	1199	-4.876	29.201	31.983	1.00	16.73		C
ANISOU	380	CE	LYS	1199	1158	2064	3134	-417	609	-645	C
ATOM	381	NZ	LYS	1199	-6.336	29.651	32.041	1.00	18.90		N1+
ANISOU	381	NZ	LYS	1199	1165	2344	3671	-341	882	-315	N1+
ATOM	382	C	LYS	1199	-1.028	26.453	27.816	1.00	9.55		C
ANISOU	382	C	LYS	1199	966	1087	1577	-74	-107	266	C
ATOM	383	O	LYS	1199	-1.825	25.741	27.205	1.00	10.78		O
ANISOU	383	O	LYS	1199	1110	1287	1700	-226	-67	132	O
ATOM	384	N	PHE	1200	0.236	26.662	27.417	1.00	9.65		N
ANISOU	384	N	PHE	1200	881	1046	1739	59	-12	228	N
ATOM	385	CA	PHE	1200	0.783	26.007	26.224	1.00	9.51		C
ANISOU	385	CA	PHE	1200	1033	914	1667	-38	-96	131	C
ATOM	386	CB	PHE	1200	1.677	27.031	25.481	1.00	10.90		C
ANISOU	386	CB	PHE	1200	1238	1013	1890	-40	246	70	C
ATOM	387	CG	PHE	1200	2.242	26.496	24.176	1.00	11.13		C
ANISOU	387	CG	PHE	1200	1111	1354	1764	-206	0	65	C
ATOM	388	CD1	PHE	1200	1.504	26.583	23.025	1.00	13.16		C
ANISOU	388	CD1	PHE	1200	1644	1518	1837	-197	-174	97	C
ATOM	389	CD2	PHE	1200	3.520	25.916	24.164	1.00	11.71		C
ANISOU	389	CD2	PHE	1200	1019	1445	1985	-237	300	-86	C
ATOM	390	CE1	PHE	1200	2.012	26.103	21.831	1.00	14.89		C
ANISOU	390	CE1	PHE	1200	2050	1726	1882	-335	-70	-90	C
ATOM	391	CE2	PHE	1200	4.027	25.420	22.956	1.00	13.84		C
ANISOU	391	CE2	PHE	1200	1660	1688	1910	-191	415	38	C
ATOM	392	CZ	PHE	1200	3.263	25.517	21.813	1.00	17.15		C
ANISOU	392	CZ	PHE	1200	1992	2511	2013	-215	175	-275	C
ATOM	393	C	PHE	1200	1.545	24.755	26.564	1.00	9.79		C
ANISOU	393	C	PHE	1200	975	1110	1633	73	-176	70	C
ATOM	394	O	PHE	1200	2.324	24.831	27.494	1.00	13.32		O
ANISOU	394	O	PHE	1200	1605	1310	2145	294	-796	-144	O

Table 1 (continued)

ATOM	395	N	VAL	1201	1.350	23.665	25.846	1.00	8.69		N
ANISOU	395	N	VAL	1201	837	1037	1428	103	-10	165	N
ATOM	396	CA	VAL	1201	2.021	22.385	26.073	1.00	8.97		C
ANISOU	396	CA	VAL	1201	730	1034	1643	25	69	125	C
ATOM	397	CB	VAL	1201	0.993	21.264	26.211	1.00	8.90		C
ANISOU	397	CB	VAL	1201	768	1076	1539	-8	-56	146	C
ATOM	398	CG1	VAL	1201	1.727	19.953	26.491	1.00	10.20		C
ANISOU	398	CG1	VAL	1201	1124	979	1770	-35	-110	165	C
ATOM	399	CG2	VAL	1201	-0.024	21.623	27.297	1.00	10.67		C
ANISOU	399	CG2	VAL	1201	877	1412	1764	-94	163	160	C
ATOM	400	C	VAL	1201	2.971	22.140	24.921	1.00	8.28		C
ANISOU	400	C	VAL	1201	765	986	1396	42	-112	55	C
ATOM	401	O	VAL	1201	2.552	22.135	23.781	1.00	9.87		O
ANISOU	401	O	VAL	1201	853	1454	1443	40	-199	265	O
ATOM	402	N	HIS	1202	4.252	21.929	25.260	1.00	8.26		N
ANISOU	402	N	HIS	1202	612	1041	1487	9	-64	-6	N
ATOM	403	CA	HIS	1202	5.267	21.752	24.232	1.00	8.05		C
ANISOU	403	CA	HIS	1202	780	960	1317	-173	-40	58	C
ATOM	404	CB	HIS	1202	6.644	22.014	24.915	1.00	8.45		C
ANISOU	404	CB	HIS	1202	573	1054	1586	-47	55	-56	C
ATOM	405	CG	HIS	1202	7.731	22.060	23.878	1.00	8.34		C
ANISOU	405	CG	HIS	1202	778	1031	1361	3	-2	51	C
ATOM	406	CD2	HIS	1202	8.419	23.162	23.434	1.00	9.11		C
ANISOU	406	CD2	HIS	1202	686	1054	1721	-130	103	-111	C
ATOM	407	ND1	HIS	1202	8.166	20.947	23.193	1.00	8.57		N
ANISOU	407	ND1	HIS	1202	891	933	1433	31	-4	-8	N
ATOM	408	CE1	HIS	1202	9.112	21.356	22.358	1.00	9.28		C
ANISOU	408	CE1	HIS	1202	970	1014	1542	-87	50	-69	C
ATOM	409	NE2	HIS	1202	9.294	22.675	22.478	1.00	9.03		N
ANISOU	409	NE2	HIS	1202	874	1004	1555	-38	112	35	N
ATOM	410	C	HIS	1202	5.219	20.388	23.570	1.00	8.20		C
ANISOU	410	C	HIS	1202	748	1076	1292	4	-132	21	C
ATOM	411	O	HIS	1202	5.258	20.290	22.331	1.00	9.39		O
ANISOU	411	O	HIS	1202	1006	1207	1357	-44	-143	-12	O
ATOM	412	N	ARG	1203	5.134	19.318	24.367	1.00	8.50		N
ANISOU	412	N	ARG	1203	800	895	1535	-80	-189	81	N
ATOM	413	CA	ARG	1203	5.038	17.905	23.939	1.00	8.97		C
ANISOU	413	CA	ARG	1203	904	1079	1427	-185	-179	-164	C
ATOM	414	CB	ARG	1203	3.994	17.653	22.830	1.00	9.19		C
ANISOU	414	CB	ARG	1203	992	1199	1299	-88	-196	-46	C
ATOM	415	CG	ARG	1203	2.627	18.191	23.233	1.00	11.55		C
ANISOU	415	CG	ARG	1203	803	1682	1905	-185	-267	-109	C
ATOM	416	CD	ARG	1203	1.545	17.734	22.217	1.00	15.13		C
ANISOU	416	CD	ARG	1203	1218	2704	1827	-315	-535	-157	C
ATOM	417	NE	ARG	1203	1.821	18.378	20.941	1.00	16.96		N
ANISOU	417	NE	ARG	1203	1331	2979	2136	-11	-601	285	N
ATOM	418	CZ	ARG	1203	1.095	18.134	19.845	1.00	19.71		C
ANISOU	418	CZ	ARG	1203	1880	3714	1895	61	-542	136	C
ATOM	419	NH1	ARG	1203	0.085	17.273	19.920	1.00	21.13		N1+
ANISOU	419	NH1	ARG	1203	2108	2943	2977	183	-1113	-537	N1+
ATOM	420	NH2	ARG	1203	1.455	18.790	18.758	1.00	29.90		N

Table 1 (continued)

ANISOU	420	NH2	ARG	1203	4222	5014	2126	135	-249	784	N
ATOM	421	C	ARG	1203	6.358	17.312	23.436	1.00	9.24		C
ANISOU	421	C	ARG	1203	1016	1026	1469	28	-226	14	C
ATOM	422	O	ARG	1203	6.398	16.092	23.222	1.00	10.31		O
ANISOU	422	O	ARG	1203	1136	1043	1738	-27	-133	-12	O
ATOM	423	N	ASP	1204	7.418	18.077	23.261	1.00	8.51		N
ANISOU	423	N	ASP	1204	881	1088	1265	94	-140	-6	N
ATOM	424	CA	ASP	1204	8.685	17.478	22.823	1.00	8.33		C
ANISOU	424	CA	ASP	1204	865	1079	1222	70	-222	-41	C
ATOM	425	CB	ASP	1204	8.742	17.401	21.281	1.00	9.88		C
ANISOU	425	CB	ASP	1204	1312	1223	1221	8	-130	-57	C
ATOM	426	CG	ASP	1204	9.837	16.494	20.766	1.00	9.76		C
ANISOU	426	CG	ASP	1204	1197	1169	1342	-94	-52	-136	C
ATOM	427	OD1	ASP	1204	10.528	15.776	21.515	1.00	10.39		O
ANISOU	427	OD1	ASP	1204	1384	987	1575	-35	-18	-154	O
ATOM	428	OD2	ASP	1204	10.046	16.516	19.521	1.00	12.40		O1-
ANISOU	428	OD2	ASP	1204	1458	1799	1455	-48	-53	-193	O1-
ATOM	429	C	ASP	1204	9.870	18.233	23.406	1.00	8.15		C
ANISOU	429	C	ASP	1204	967	800	1329	-65	-33	-106	C
ATOM	430	O	ASP	1204	10.831	18.547	22.712	1.00	9.16		O
ANISOU	430	O	ASP	1204	1077	1059	1346	-78	89	-126	O
ATOM	431	N	LEU	1205	9.803	18.514	24.721	1.00	7.83		N
ANISOU	431	N	LEU	1205	948	767	1260	31	-162	-19	N
ATOM	432	CA	LEU	1205	10.948	19.175	25.332	1.00	7.58		C
ANISOU	432	CA	LEU	1205	745	879	1257	-27	-46	-56	C
ATOM	433	CB	LEU	1205	10.526	19.716	26.691	1.00	8.62		C
ANISOU	433	CB	LEU	1205	908	1196	1169	-77	-58	-71	C
ATOM	434	CG	LEU	1205	11.597	20.490	27.458	1.00	8.64		C
ANISOU	434	CG	LEU	1205	1103	898	1283	-162	-169	44	C
ATOM	435	CD1	LEU	1205	12.057	21.746	26.699	1.00	10.45		C
ANISOU	435	CD1	LEU	1205	1488	929	1555	-37	-62	245	C
ATOM	436	CD2	LEU	1205	11.065	20.883	28.815	1.00	9.85		C
ANISOU	436	CD2	LEU	1205	1513	995	1236	-94	-157	-45	C
ATOM	437	C	LEU	1205	12.103	18.187	25.445	1.00	7.78		C
ANISOU	437	C	LEU	1205	847	915	1195	-77	-48	-69	C
ATOM	438	O	LEU	1205	11.929	17.053	25.896	1.00	8.78		O
ANISOU	438	O	LEU	1205	1016	969	1353	69	-6	129	O
ATOM	439	N	ALA	1206	13.284	18.613	25.050	1.00	7.99		N
ANISOU	439	N	ALA	1206	763	987	1284	85	-59	-66	N
ATOM	440	CA	ALA	1206	14.508	17.815	25.031	1.00	7.84		C
ANISOU	440	CA	ALA	1206	825	920	1233	64	57	-173	C
ATOM	441	CB	ALA	1206	14.422	16.697	23.983	1.00	8.71		C
ANISOU	441	CB	ALA	1206	990	977	1343	33	-67	-280	C
ATOM	442	C	ALA	1206	15.639	18.765	24.744	1.00	7.56		C
ANISOU	442	C	ALA	1206	886	909	1079	-19	-202	-64	C
ATOM	443	O	ALA	1206	15.400	19.828	24.142	1.00	8.39		O
ANISOU	443	O	ALA	1206	949	946	1291	79	-133	30	O
ATOM	444	N	ALA	1207	16.887	18.448	25.103	1.00	7.51		N
ANISOU	444	N	ALA	1207	791	913	1151	4	-19	-36	N
ATOM	445	CA	ALA	1207	17.985	19.371	24.821	1.00	8.23		C
ANISOU	445	CA	ALA	1207	822	1046	1260	-65	-204	138	C

Table 1 (continued)

ATOM	446	CB	ALA	1207	19.280	18.819	25.417	1.00	8.64		C
ANISOU	446	CB	ALA	1207	827	1297	1158	101	-87	-18	C
ATOM	447	C	ALA	1207	18.126	19.644	23.334	1.00	7.72		C
ANISOU	447	C	ALA	1207	837	823	1272	44	-33	78	C
ATOM	448	O	ALA	1207	18.480	20.756	22.948	1.00	8.46		O
ANISOU	448	O	ALA	1207	884	977	1354	-138	-244	158	O
ATOM	449	N	ARG	1208	17.854	18.654	22.450	1.00	8.02		N
ANISOU	449	N	ARG	1208	882	896	1271	81	-93	-24	N
ATOM	450	CA	ARG	1208	17.970	18.859	21.024	1.00	8.31		C
ANISOU	450	CA	ARG	1208	972	914	1273	137	-19	-8	C
ATOM	451	CB	ARG	1208	17.704	17.520	20.279	1.00	9.14		C
ANISOU	451	CB	ARG	1208	1153	1034	1287	87	55	-123	C
ATOM	452	CG	ARG	1208	16.295	16.977	20.491	1.00	8.97		C
ANISOU	452	CG	ARG	1208	1218	1107	1082	-22	28	-102	C
ATOM	453	CD	ARG	1208	16.010	15.687	19.637	1.00	10.16		C
ANISOU	453	CD	ARG	1208	1579	861	1420	47	55	-148	C
ATOM	454	NE	ARG	1208	14.668	15.224	20.123	1.00	10.44		N
ANISOU	454	NE	ARG	1208	1579	945	1442	-97	-145	64	N
ATOM	455	CZ	ARG	1208	14.463	14.444	21.146	1.00	9.46		C
ANISOU	455	CZ	ARG	1208	1314	609	1671	-164	-283	-37	C
ATOM	456	NH1	ARG	1208	15.533	13.958	21.837	1.00	9.90		N1+
ANISOU	456	NH1	ARG	1208	1388	1079	1296	-20	-196	-48	N1+
ATOM	457	NH2	ARG	1208	13.214	14.133	21.501	1.00	11.17		N
ANISOU	457	NH2	ARG	1208	1318	1052	1874	-312	-143	-132	N
ATOM	458	C	ARG	1208	17.012	19.904	20.500	1.00	8.35		C
ANISOU	458	C	ARG	1208	878	941	1352	12	29	149	C
ATOM	459	O	ARG	1208	17.207	20.425	19.402	1.00	8.95		O
ANISOU	459	O	ARG	1208	1118	1110	1172	73	14	13	O
ATOM	460	N	ASN	1209	15.949	20.212	21.296	1.00	7.95		N
ANISOU	460	N	ASN	1209	938	854	1228	60	-37	4	N
ATOM	461	CA	ASN	1209	14.881	21.099	20.862	1.00	8.64		C
ANISOU	461	CA	ASN	1209	851	894	1538	37	-232	-102	C
ATOM	462	CB	ASN	1209	13.519	20.416	21.139	1.00	8.68		C
ANISOU	462	CB	ASN	1209	966	935	1395	-38	5	-217	C
ATOM	463	CG	ASN	1209	13.264	19.300	20.134	1.00	8.67		C
ANISOU	463	CG	ASN	1209	1028	966	1301	3	-156	-154	C
ATOM	464	OD1	ASN	1209	13.698	19.404	18.971	1.00	10.43		O
ANISOU	464	OD1	ASN	1209	1434	1224	1306	-224	-74	-219	O
ATOM	465	ND2	ASN	1209	12.593	18.252	20.582	1.00	9.67		N
ANISOU	465	ND2	ASN	1209	1118	1017	1539	-120	-59	-146	N
ATOM	466	C	ASN	1209	14.958	22.490	21.525	1.00	7.70		C
ANISOU	466	C	ASN	1209	1021	816	1087	43	-230	29	C
ATOM	467	O	ASN	1209	13.991	23.253	21.454	1.00	8.89		O
ANISOU	467	O	ASN	1209	1018	907	1453	95	-116	0	O
ATOM	468	N	CYS	1210	16.102	22.774	22.131	1.00	7.98		N
ANISOU	468	N	CYS	1210	1022	846	1163	-64	-172	22	N
ATOM	469	CA	CYS	1210	16.409	24.089	22.689	1.00	7.90		C
ANISOU	469	CA	CYS	1210	965	881	1157	-100	-60	-82	C
ATOM	470	CB	CYS	1210	16.730	24.063	24.188	1.00	8.44		C
ANISOU	470	CB	CYS	1210	1084	1012	1110	-129	-45	51	C
ATOM	471	SG	CYS	1210	15.336	23.400	25.174	1.00	9.02		S

Table 1 (continued)

ANISOU	471	SG	CYS	1210	1127	996	1304	-70	-28	34	S
ATOM	472	C	CYS	1210	17.616	24.640	21.940	1.00	7.69		C
ANISOU	472	C	CYS	1210	911	922	1088	-24	-108	-15	C
ATOM	473	O	CYS	1210	18.462	23.813	21.570	1.00	8.85		O
ANISOU	473	O	CYS	1210	924	1014	1424	91	16	106	O
ATOM	474	N	MET	1211	17.671	25.946	21.748	1.00	8.01		N
ANISOU	474	N	MET	1211	890	894	1261	-52	40	11	N
ATOM	475	CA	MET	1211	18.786	26.581	21.036	1.00	8.30		C
ANISOU	475	CA	MET	1211	953	1059	1141	-136	-99	99	C
ATOM	476	CB	MET	1211	18.263	27.341	19.806	1.00	9.78		C
ANISOU	476	CB	MET	1211	1426	935	1355	-94	-266	182	C
ATOM	477	CG	MET	1211	17.450	26.482	18.851	1.00	9.86		C
ANISOU	477	CG	MET	1211	1203	1205	1337	-39	-188	-64	C
ATOM	478	SD	MET	1211	18.419	25.175	18.068	1.00	10.93		S
ANISOU	478	SD	MET	1211	1372	1318	1462	111	-138	-36	S
ATOM	479	CE	MET	1211	17.287	23.785	18.116	1.00	13.56		C
ANISOU	479	CE	MET	1211	1959	1293	1902	-163	-462	-123	C
ATOM	480	C	MET	1211	19.529	27.531	21.945	1.00	8.50		C
ANISOU	480	C	MET	1211	903	1025	1303	-31	-21	-9	C
ATOM	481	O	MET	1211	19.002	27.946	22.983	1.00	10.04		O
ANISOU	481	O	MET	1211	1000	1342	1474	-2	-35	-371	O
ATOM	482	N	LEU	1212	20.765	27.865	21.554	1.00	9.06		N
ANISOU	482	N	LEU	1212	1026	1033	1385	-221	-41	45	N
ATOM	483	CA	LEU	1212	21.597	28.737	22.391	1.00	10.03		C
ANISOU	483	CA	LEU	1212	1156	1213	1442	-256	-132	-87	C
ATOM	484	CB	LEU	1212	22.705	27.878	23.035	1.00	13.63		C
ANISOU	484	CB	LEU	1212	1011	1958	2211	237	-266	-304	C
ATOM	485	CG	LEU	1212	23.637	28.423	24.087	1.00	15.76		C
ANISOU	485	CG	LEU	1212	1424	2489	2077	368	-418	-348	C
ATOM	486	CD1	LEU	1212	22.863	28.789	25.349	1.00	15.92		C
ANISOU	486	CD1	LEU	1212	1866	2489	1695	-122	-140	207	C
ATOM	487	CD2	LEU	1212	24.717	27.429	24.478	1.00	16.72		C
ANISOU	487	CD2	LEU	1212	1874	2414	2065	231	-606	407	C
ATOM	488	C	LEU	1212	22.142	29.882	21.552	1.00	10.90		C
ANISOU	488	C	LEU	1212	1049	1456	1636	-516	100	-268	C
ATOM	489	O	LEU	1212	22.746	29.611	20.516	1.00	12.77		O
ANISOU	489	O	LEU	1212	1273	1775	1805	-560	323	-209	O
ATOM	490	N	ASP	1213	21.951	31.117	21.979	1.00	11.62		N
ANISOU	490	N	ASP	1213	1331	1292	1792	-419	-136	-64	N
ATOM	491	CA	ASP	1213	22.420	32.266	21.164	1.00	12.65		C
ANISOU	491	CA	ASP	1213	1574	1373	1860	-431	146	-36	C
ATOM	492	CB	ASP	1213	21.380	33.379	21.233	1.00	13.17		C
ANISOU	492	CB	ASP	1213	1760	1411	1833	-273	-87	-12	C
ATOM	493	CG	ASP	1213	21.315	34.180	22.519	1.00	12.24		C
ANISOU	493	CG	ASP	1213	1512	1333	1805	-256	13	75	C
ATOM	494	OD1	ASP	1213	22.175	34.055	23.416	1.00	12.12		O
ANISOU	494	OD1	ASP	1213	1625	1254	1725	-294	54	9	O
ATOM	495	OD2	ASP	1213	20.355	34.995	22.642	1.00	14.98		O1-
ANISOU	495	OD2	ASP	1213	1920	1420	2351	19	32	-35	O1-
ATOM	496	C	ASP	1213	23.804	32.701	21.594	1.00	13.67		C
ANISOU	496	C	ASP	1213	1627	1406	2160	-495	70	5	C

Table 1 (continued)

ATOM	497	O	ASP	1213	24.487	32.112	22.424	1.00	13.82		O
ANISOU	497	O	ASP	1213	1410	1557	2282	-255	184	-96	O
ATOM	498	N	GLU	1214	24.252	33.811	20.976	1.00	14.40		N
ANISOU	498	N	GLU	1214	2006	1555	1911	-843	182	-164	N
ATOM	499	CA	GLU	1214	25.646	34.223	21.170	1.00	15.62		C
ANISOU	499	CA	GLU	1214	1872	1843	2218	-824	393	-273	C
ATOM	500	CB	GLU	1214	25.995	35.297	20.115	1.00	21.19		C
ANISOU	500	CB	GLU	1214	2885	2457	2710	-1232	895	76	C
ATOM	501	CG	GLU	1214	25.488	36.672	20.466	1.00	25.38		C
ANISOU	501	CG	GLU	1214	4622	2231	2789	-893	588	425	C
ATOM	502	CD	GLU	1214	24.041	36.878	20.079	1.00	31.60		C
ANISOU	502	CD	GLU	1214	4746	3140	4121	178	586	-131	C
ATOM	503	OE1	GLU	1214	23.623	38.060	19.972	1.00	55.89		O1-
ANISOU	503	OE1	GLU	1214	7816	4393	9025	2739	465	-1249	O1-
ATOM	504	OE2	GLU	1214	23.347	35.869	19.889	1.00	42.70		O
ANISOU	504	OE2	GLU	1214	4924	5355	5944	-1189	-279	-923	O
ATOM	505	C	GLU	1214	25.921	34.728	22.573	1.00	15.46		C
ANISOU	505	C	GLU	1214	1486	1966	2423	-638	235	-488	C
ATOM	506	O	GLU	1214	27.115	34.824	22.956	1.00	17.86		O
ANISOU	506	O	GLU	1214	1554	2303	2931	-681	149	-569	O
ATOM	507	N	LYS	1215	24.903	35.052	23.340	1.00	13.55		N
ANISOU	507	N	LYS	1215	1606	1388	2154	-368	167	-147	N
ATOM	508	CA	LYS	1215	25.049	35.440	24.752	1.00	13.47		C
ANISOU	508	CA	LYS	1215	1539	1432	2145	-288	-38	-115	C
ATOM	509	CB	LYS	1215	24.091	36.594	25.093	1.00	15.71		C
ANISOU	509	CB	LYS	1215	2050	1671	2247	-78	255	-192	C
ATOM	510	CG	LYS	1215	24.427	37.817	24.234	1.00	22.20		C
ANISOU	510	CG	LYS	1215	3128	1481	3825	65	607	217	C
ATOM	511	CD	LYS	1215	23.463	38.948	24.570	1.00	25.70		C
ANISOU	511	CD	LYS	1215	3764	2273	3727	952	231	323	C
ATOM	512	CE	LYS	1215	23.947	40.229	23.889	1.00	28.08		C
ANISOU	512	CE	LYS	1215	4177	2139	4353	1324	167	675	C
ATOM	513	NZ	LYS	1215	22.996	41.318	24.282	1.00	33.64		N1+
ANISOU	513	NZ	LYS	1215	5337	2734	4710	2102	636	789	N1+
ATOM	514	C	LYS	1215	24.802	34.275	25.709	1.00	12.61		C
ANISOU	514	C	LYS	1215	1099	1551	2141	-591	95	-133	C
ATOM	515	O	LYS	1215	24.725	34.464	26.927	1.00	14.30		O
ANISOU	515	O	LYS	1215	1611	1719	2103	-355	-114	-116	O
ATOM	516	N	PHE	1216	24.692	33.063	25.167	1.00	12.96		N
ANISOU	516	N	PHE	1216	1206	1457	2260	-504	-243	-69	N
ATOM	517	CA	PHE	1216	24.436	31.824	25.908	1.00	13.16		C
ANISOU	517	CA	PHE	1216	1140	1515	2346	-170	-204	218	C
ATOM	518	CB	PHE	1216	25.569	31.516	26.895	1.00	15.70		C
ANISOU	518	CB	PHE	1216	1201	2058	2707	-161	-467	46	C
ATOM	519	CG	PHE	1216	26.891	31.449	26.127	1.00	17.27		C
ANISOU	519	CG	PHE	1216	1156	2576	2829	-321	-414	-411	C
ATOM	520	CD1	PHE	1216	27.208	30.377	25.303	1.00	19.84		C
ANISOU	520	CD1	PHE	1216	1545	2210	3783	-190	-90	-450	C
ATOM	521	CD2	PHE	1216	27.808	32.490	26.240	1.00	18.93		C
ANISOU	521	CD2	PHE	1216	1561	2467	3166	-531	25	-375	C
ATOM	522	CE1	PHE	1216	28.408	30.319	24.593	1.00	20.84		C

Table 1 (continued)

ANISOU	522	CE1	PHE	1216	1873	2345	3701	-152	202	-370	C
ATOM	523	CE2	PHE	1216	29.030	32.455	25.542	1.00	21.11		C
ANISOU	523	CE2	PHE	1216	1538	2657	3825	-400	237	-531	C
ATOM	524	CZ	PHE	1216	29.326	31.366	24.720	1.00	21.59		C
ANISOU	524	CZ	PHE	1216	1842	2564	3796	-294	237	-448	C
ATOM	525	C	PHE	1216	23.079	31.886	26.620	1.00	12.67		C
ANISOU	525	C	PHE	1216	1148	1864	1801	-282	-339	80	C
ATOM	526	O	PHE	1216	22.887	31.344	27.697	1.00	13.17		O
ANISOU	526	O	PHE	1216	1345	1716	1942	-203	-295	174	O
ATOM	527	N	THR	1217	22.139	32.577	25.942	1.00	11.34		N
ANISOU	527	N	THR	1217	1117	1405	1785	-227	-235	-109	N
ATOM	528	CA	THR	1217	20.748	32.489	26.326	1.00	11.25		C
ANISOU	528	CA	THR	1217	1099	1214	1962	-306	-189	-135	C
ATOM	529	CB	THR	1217	19.964	33.743	25.918	1.00	13.02		C
ANISOU	529	CB	THR	1217	1167	1141	2640	-295	-151	17	C
ATOM	530	OG1	THR	1217	20.534	34.910	26.615	1.00	17.48		O
ANISOU	530	OG1	THR	1217	1641	1318	3683	-382	-414	-354	O
ATOM	531	CG2	THR	1217	18.511	33.697	26.348	1.00	12.25		C
ANISOU	531	CG2	THR	1217	1251	1291	2111	-139	22	-72	C
ATOM	532	C	THR	1217	20.134	31.272	25.660	1.00	9.65		C
ANISOU	532	C	THR	1217	1056	1138	1474	-192	-75	-12	C
ATOM	533	O	THR	1217	20.224	31.123	24.451	1.00	10.32		O
ANISOU	533	O	THR	1217	1177	1239	1504	-176	-86	0	O
ATOM	534	N	VAL	1218	19.507	30.431	26.484	1.00	9.35		N
ANISOU	534	N	VAL	1218	1051	1058	1444	-168	-235	24	N
ATOM	535	CA	VAL	1218	18.792	29.248	25.986	1.00	9.25		C
ANISOU	535	CA	VAL	1218	982	878	1655	-27	-247	40	C
ATOM	536	CB	VAL	1218	18.754	28.133	27.040	1.00	9.89		C
ANISOU	536	CB	VAL	1218	1344	996	1418	-61	-137	65	C
ATOM	537	CG1	VAL	1218	18.078	26.863	26.439	1.00	11.25		C
ANISOU	537	CG1	VAL	1218	1510	1138	1626	-369	123	59	C
ATOM	538	CG2	VAL	1218	20.128	27.780	27.554	1.00	12.65		C
ANISOU	538	CG2	VAL	1218	1693	1280	1833	55	-536	232	C
ATOM	539	C	VAL	1218	17.368	29.612	25.619	1.00	7.89		C
ANISOU	539	C	VAL	1218	870	833	1295	-12	-6	-52	C
ATOM	540	O	VAL	1218	16.692	30.239	26.418	1.00	10.44		O
ANISOU	540	O	VAL	1218	1137	1341	1489	-71	79	-310	O
ATOM	541	N	LYS	1219	16.969	29.195	24.425	1.00	8.44		N
ANISOU	541	N	LYS	1219	834	1019	1352	-121	-40	-95	N
ATOM	542	CA	LYS	1219	15.569	29.383	23.995	1.00	9.19		C
ANISOU	542	CA	LYS	1219	890	1015	1587	-91	-152	-186	C
ATOM	543	CB	LYS	1219	15.514	30.233	22.731	1.00	12.40		C
ANISOU	543	CB	LYS	1219	1210	1276	2223	-239	-501	362	C
ATOM	544	CG	LYS	1219	16.165	31.598	23.150	1.00	22.15		C
ANISOU	544	CG	LYS	1219	2301	1279	4838	-814	116	300	C
ATOM	545	CD	LYS	1219	15.729	32.750	22.403	1.00	20.39		C
ANISOU	545	CD	LYS	1219	2107	1248	4393	-473	65	-144	C
ATOM	546	CE	LYS	1219	16.685	33.919	22.727	1.00	15.19		C
ANISOU	546	CE	LYS	1219	2066	1127	2578	-496	556	-9	C
ATOM	547	NZ	LYS	1219	15.983	34.885	23.611	1.00	12.39		N1+
ANISOU	547	NZ	LYS	1219	1581	1505	1621	-25	29	277	N1+

Table 1 (continued)

ATOM	548	C	LYS	1219	14.948	28.031	23.765	1.00	8.58		C
ANISOU	548	C	LYS	1219	888	1007	1366	-69	-151	-139	C
ATOM	549	O	LYS	1219	15.477	27.209	22.996	1.00	9.41		O
ANISOU	549	O	LYS	1219	1008	1061	1507	-29	10	-168	O
ATOM	550	N	VAL	1220	13.817	27.787	24.424	1.00	8.56		N
ANISOU	550	N	VAL	1220	896	944	1415	-25	-140	91	N
ATOM	551	CA	VAL	1220	12.976	26.631	24.091	1.00	8.95		C
ANISOU	551	CA	VAL	1220	1058	1062	1281	-184	-148	116	C
ATOM	552	CB	VAL	1220	11.800	26.498	25.067	1.00	9.18		C
ANISOU	552	CB	VAL	1220	1095	1171	1223	-171	-82	79	C
ATOM	553	CG1	VAL	1220	10.862	25.383	24.638	1.00	10.40		C
ANISOU	553	CG1	VAL	1220	1225	1186	1541	-313	-185	271	C
ATOM	554	CG2	VAL	1220	12.339	26.259	26.507	1.00	10.54		C
ANISOU	554	CG2	VAL	1220	1542	1195	1266	-49	-273	303	C
ATOM	555	C	VAL	1220	12.512	26.846	22.676	1.00	8.31		C
ANISOU	555	C	VAL	1220	957	950	1249	29	-101	37	C
ATOM	556	O	VAL	1220	11.917	27.897	22.370	1.00	9.16		O
ANISOU	556	O	VAL	1220	1224	872	1384	93	-109	94	O
ATOM	557	N	ALA	1221	12.762	25.896	21.785	1.00	8.29		N
ANISOU	557	N	ALA	1221	934	963	1253	14	-153	47	N
ATOM	558	CA	ALA	1221	12.457	26.025	20.371	1.00	8.20		C
ANISOU	558	CA	ALA	1221	973	956	1188	-83	-107	-31	C
ATOM	559	CB	ALA	1221	13.744	26.054	19.557	1.00	9.29		C
ANISOU	559	CB	ALA	1221	1045	1024	1460	29	17	109	C
ATOM	560	C	ALA	1221	11.494	24.901	19.979	1.00	8.97		C
ANISOU	560	C	ALA	1221	1151	1011	1247	-162	-187	131	C
ATOM	561	O	ALA	1221	10.791	24.379	20.854	1.00	9.47		O
ANISOU	561	O	ALA	1221	1172	1067	1358	-169	-133	140	O
ATOM	562	N	ASP	1222	11.430	24.531	18.709	1.00	9.14		N
ANISOU	562	N	ASP	1222	1233	980	1258	-45	-271	-65	N
ATOM	563	CA	ASP	1222	10.669	23.351	18.299	1.00	9.81		C
ANISOU	563	CA	ASP	1222	1107	1014	1605	-113	-209	0	C
ATOM	564	CB	ASP	1222	11.309	22.059	18.844	1.00	10.51		C
ANISOU	564	CB	ASP	1222	1228	987	1779	71	-56	22	C
ATOM	565	CG	ASP	1222	10.606	20.850	18.310	1.00	11.12		C
ANISOU	565	CG	ASP	1222	1573	1064	1589	85	-305	33	C
ATOM	566	OD1	ASP	1222	10.236	20.848	17.133	1.00	12.27		O
ANISOU	566	OD1	ASP	1222	1786	1256	1620	159	-236	16	O
ATOM	567	OD2	ASP	1222	10.381	19.934	19.132	1.00	10.87		O1-
ANISOU	567	OD2	ASP	1222	1495	1099	1534	-134	-149	-28	O1-
ATOM	568	C	ASP	1222	9.227	23.398	18.765	1.00	9.36		C
ANISOU	568	C	ASP	1222	1104	1166	1286	9	-188	52	C
ATOM	569	O	ASP	1222	8.670	22.447	19.286	1.00	10.04		O
ANISOU	569	O	ASP	1222	1166	1153	1497	-107	-211	-7	O
ATOM	570	N	PHE	1223	8.554	24.546	18.566	1.00	9.78		N
ANISOU	570	N	PHE	1223	1249	1167	1301	19	-301	-58	N
ATOM	571	CA	PHE	1223	7.126	24.596	18.848	1.00	11.22		C
ANISOU	571	CA	PHE	1223	1270	1327	1665	242	-190	129	C
ATOM	572	CB	PHE	1223	6.800	25.003	20.296	1.00	12.10		C
ANISOU	572	CB	PHE	1223	1404	1370	1822	132	28	4	C
ATOM	573	CG	PHE	1223	7.141	26.462	20.545	1.00	12.79		C

Table 1 (continued)

ANISOU	573	CG	PHE	1223	1373	1503	1983	20	-21	-60	C
ATOM	574	CD1	PHE	1223	8.413	26.895	20.858	1.00	15.18		C
ANISOU	574	CD1	PHE	1223	1630	1870	2268	-16	-400	-538	C
ATOM	575	CD2	PHE	1223	6.158	27.442	20.458	1.00	14.32		C
ANISOU	575	CD2	PHE	1223	1937	1363	2141	226	-587	-39	C
ATOM	576	CE1	PHE	1223	8.694	28.271	21.060	1.00	16.28		C
ANISOU	576	CE1	PHE	1223	1717	1810	2658	97	-63	-858	C
ATOM	577	CE2	PHE	1223	6.384	28.780	20.632	1.00	13.39		C
ANISOU	577	CE2	PHE	1223	1758	1379	1949	-153	-177	91	C
ATOM	578	CZ	PHE	1223	7.672	29.202	20.937	1.00	14.68		C
ANISOU	578	CZ	PHE	1223	1540	1837	2203	-63	13	100	C
ATOM	579	C	PHE	1223	6.499	25.557	17.832	1.00	12.18		C
ANISOU	579	C	PHE	1223	1353	1299	1976	68	-414	190	C
ATOM	580	O	PHE	1223	7.186	26.344	17.185	1.00	12.98		O
ANISOU	580	O	PHE	1223	1629	1376	1927	38	-313	236	O
ATOM	581	N	GLY	1224	5.178	25.486	17.727	1.00	12.75		N
ANISOU	581	N	GLY	1224	1288	1506	2051	282	-397	14	N
ATOM	582	CA	GLY	1224	4.472	26.347	16.791	1.00	15.36		C
ANISOU	582	CA	GLY	1224	1505	1773	2560	161	-569	446	C
ATOM	583	C	GLY	1224	4.994	26.137	15.380	1.00	15.88		C
ANISOU	583	C	GLY	1224	1935	1810	2290	-162	-798	422	C
ATOM	584	O	GLY	1224	5.197	25.010	14.894	1.00	15.10		O
ANISOU	584	O	GLY	1224	1937	1777	2024	-281	-825	432	O
ATOM	585	N	LEU	1225	5.223	27.257	14.691	1.00	16.25		N
ANISOU	585	N	LEU	1225	1960	1782	2435	16	-873	500	N
ATOM	586	CA	LEU	1225	5.678	27.210	13.299	1.00	16.56		C
ANISOU	586	CA	LEU	1225	2361	1615	2314	32	-1013	735	C
ATOM	587	CB	LEU	1225	5.665	28.616	12.672	1.00	18.65		C
ANISOU	587	CB	LEU	1225	2170	1571	3347	-358	-939	990	C
ATOM	588	CG	LEU	1225	4.313	29.329	12.779	1.00	20.58		C
ANISOU	588	CG	LEU	1225	2539	1648	3634	49	-1527	840	C
ATOM	589	CD1	LEU	1225	4.459	30.677	12.053	1.00	23.87		C
ANISOU	589	CD1	LEU	1225	3188	2090	3792	25	-1392	1309	C
ATOM	590	CD2	LEU	1225	3.140	28.533	12.235	1.00	21.01		C
ANISOU	590	CD2	LEU	1225	2162	2220	3601	98	-1081	290	C
ATOM	591	C	LEU	1225	7.067	26.601	13.187	1.00	14.92		C
ANISOU	591	C	LEU	1225	2249	1610	1808	-188	-765	743	C
ATOM	592	O	LEU	1225	7.453	26.251	12.063	1.00	18.36		O
ANISOU	592	O	LEU	1225	2890	2237	1848	206	-1051	283	O
ATOM	593	N	ALA	1226	7.784	26.482	14.297	1.00	13.46		N
ANISOU	593	N	ALA	1226	2067	1314	1733	-21	-735	382	N
ATOM	594	CA	ALA	1226	9.141	25.913	14.271	1.00	14.72		C
ANISOU	594	CA	ALA	1226	1934	1506	2151	-107	-469	469	C
ATOM	595	CB	ALA	1226	10.008	26.733	15.208	1.00	17.51		C
ANISOU	595	CB	ALA	1226	1649	1965	3039	-789	-314	500	C
ATOM	596	C	ALA	1226	9.176	24.424	14.663	1.00	13.09		C
ANISOU	596	C	ALA	1226	1739	1553	1680	27	-474	404	C
ATOM	597	O	ALA	1226	10.254	23.844	14.810	1.00	13.67		O
ANISOU	597	O	ALA	1226	1791	1643	1761	159	-341	229	O
ATOM	598	N	AARG	1227	8.007	23.781	14.834	0.70	12.96		N
ANISOU	598	N	AARG	1227	1867	1510	1547	-237	-607	260	N

Table 1 (continued)

ATOM	599	N	BARG	1227	8.009	23.783	14.837	0.30	12.98		N
ANISOU	599	N	BRAG	1227	1842	1493	1595	-143	-491	263	N
ATOM	600	CA	AARG	1227	7.916	22.391	15.255	0.70	13.35		C
ANISOU	600	CA	AARG	1227	1947	1444	1680	111	-102	229	C
ATOM	601	CA	BRAG	1227	7.879	22.379	15.220	0.30	14.10		C
ANISOU	601	CA	BRAG	1227	2066	1436	1856	70	-48	210	C
ATOM	602	CB	AARG	1227	6.476	22.060	15.661	0.70	18.56		C
ANISOU	602	CB	AARG	1227	2435	2038	2580	11	633	768	C
ATOM	603	CB	BARG	1227	6.430	21.973	15.517	0.30	17.88		C
ANISOU	603	CB	BARG	1227	2394	1541	2859	-154	521	165	C
ATOM	604	CG	AARG	1227	6.225	20.627	16.034	0.70	22.87		C
ANISOU	604	CG	AARG	1227	2869	1892	3927	-735	273	116	C
ATOM	605	CG	BARG	1227	6.192	20.861	16.521	0.30	21.30		C
ANISOU	605	CG	BARG	1227	2833	1802	3457	-103	772	523	C
ATOM	606	CD	AARG	1227	4.769	20.276	16.112	0.70	25.14		C
ANISOU	606	CD	AARG	1227	2759	2719	4073	-404	724	894	C
ATOM	607	CD	BARG	1227	4.795	20.264	16.442	0.30	22.46		C
ANISOU	607	CD	BARG	1227	2809	1970	3756	-98	466	1270	C
ATOM	608	NE	AARG	1227	3.873	21.164	15.357	0.70	31.62		N
ANISOU	608	NE	AARG	1227	3492	3426	5097	118	-325	524	N
ATOM	609	NE	BARG	1227	4.705	18.886	16.922	0.30	15.60		N
ANISOU	609	NE	BARG	1227	1815	1434	2680	448	275	501	N
ATOM	610	CZ	AARG	1227	2.754	20.560	14.919	0.70	37.82		C
ANISOU	610	CZ	AARG	1227	4182	4963	5224	-650	-908	773	C
ATOM	611	CZ	BRAG	1227	3.806	17.974	16.608	0.30	13.18		C
ANISOU	611	CZ	BRAG	1227	1294	1721	1992	490	-91	1253	C
ATOM	612	NH1AARG		1227	2.646	19.273	15.234	0.70	38.45		N1+
ANISOU	612	NH1AARG		1227	4662	5574	4371	-1905	-1517	1503	N1+
ATOM	613	NH1BARG		1227	2.823	18.268	15.753	0.30	20.09		N1+
ANISOU	613	NH1BARG		1227	2683	2678	2274	796	-896	1484	N1+
ATOM	614	NH2AARG		1227	1.836	21.187	14.230	0.70	42.04		N
ANISOU	614	NH2AARG		1227	3623	7166	5186	-1835	-479	3431	N
ATOM	615	NH2BARG		1227	3.811	16.729	17.106	0.30	11.30		N
ANISOU	615	NH2BARG		1227	1212	1798	1284	300	131	1246	N
ATOM	616	C	AARG	1227	8.329	21.438	14.150	0.70	13.98		C
ANISOU	616	C	AARG	1227	1836	1758	1720	-57	-432	-124	C
ATOM	617	C	BRAG	1227	8.412	21.474	14.115	0.30	14.02		C
ANISOU	617	C	BRAG	1227	1947	1667	1712	-69	-287	13	C
ATOM	618	O	AARG	1227	7.915	21.637	13.004	0.70	16.02		O
ANISOU	618	O	AARG	1227	2321	1990	1777	-205	-711	-18	O
ATOM	619	O	BRAG	1227	8.174	21.719	12.932	0.30	16.70		O
ANISOU	619	O	BARG	1227	2516	2050	1781	-23	-754	-97	O
ATOM	620	N	ASP	1228	9.136	20.419	14.508	1.00	14.10		N
ANISOU	620	N	ASP	1228	1981	1697	1680	74	-248	-132	N
ATOM	621	CA	ASP	1228	9.529	19.404	13.544	1.00	15.18		C
ANISOU	621	CA	ASP	1228	2764	1480	1525	-137	70	21	C
ATOM	622	CB	ASP	1228	10.502	19.943	12.486	1.00	16.06		C
ANISOU	622	CB	ASP	1228	2709	1991	1404	-614	-57	-200	C

Table 1 (continued)

ATOM	623	CG	ASP	1228	10.393	19.298	11.119	1.00	18.55		C
ANISOU	623	CG	ASP	1228	3652	1938	1458	-961	117	-210	C
ATOM	624	OD1	ASP	1228	10.147	18.076	11.050	1.00	18.61		O
ANISOU	624	OD1	ASP	1228	3446	1850	1776	-725	-476	-187	O
ATOM	625	OD2	ASP	1228	10.561	20.019	10.103	1.00	17.47		O1-
ANISOU	625	OD2	ASP	1228	3409	1803	1426	-344	76	-159	O1-
ATOM	626	C	ASP	1228	10.175	18.245	14.299	1.00	14.24		C
ANISOU	626	C	ASP	1228	2207	1621	1583	6	-94	-163	C
ATOM	627	O	ASP	1228	10.201	18.283	15.537	1.00	15.70		O
ANISOU	627	O	ASP	1228	2652	1753	1560	109	-284	-164	O
ATOM	628	N	MET	1229	10.689	17.248	13.590	1.00	16.18		N
ANISOU	628	N	MET	1229	2186	2048	1914	176	-83	-451	N
ATOM	629	CA	MET	1229	11.591	16.243	14.124	1.00	14.87		C
ANISOU	629	CA	MET	1229	2211	1808	1633	112	-88	-433	C
ATOM	630	CB	MET	1229	11.271	14.790	13.649	1.00	17.55		C
ANISOU	630	CB	MET	1229	2673	2068	1928	-65	432	-1018	C
ATOM	631	CG	MET	1229	9.875	14.483	14.150	1.00	23.83		C
ANISOU	631	CG	MET	1229	2394	3061	3599	-418	369	-1656	C
ATOM	632	SD	MET	1229	9.387	12.758	13.822	1.00	26.58		S
ANISOU	632	SD	MET	1229	3407	2962	3730	-746	-480	-273	S
ATOM	633	CE	MET	1229	11.066	12.176	13.470	1.00	14.36		C
ANISOU	633	CE	MET	1229	3344	1016	1096	-932	-684	-101	C
ATOM	634	C	MET	1229	12.994	16.564	13.677	1.00	14.49		C
ANISOU	634	C	MET	1229	2273	1829	1404	175	-82	-234	C
ATOM	635	O	MET	1229	13.213	16.412	12.472	1.00	17.29		O
ANISOU	635	O	MET	1229	2995	2172	1401	-416	132	-193	O
ATOM	636	N	TYR	1230	13.916	16.982	14.526	1.00	12.95		N
ANISOU	636	N	TYR	1230	2158	1296	1466	58	-52	-56	N
ATOM	637	CA	TYR	1230	15.215	17.476	14.087	1.00	13.52		C
ANISOU	637	CA	TYR	1230	2254	1382	1500	100	89	-6	C
ATOM	638	CB	TYR	1230	15.566	18.760	14.847	1.00	13.61		C
ANISOU	638	CB	TYR	1230	2075	1242	1856	62	53	50	C
ATOM	639	CG	TYR	1230	14.670	19.906	14.441	1.00	14.14		C
ANISOU	639	CG	TYR	1230	2268	1291	1816	100	134	135	C
ATOM	640	CD1	TYR	1230	14.882	20.541	13.207	1.00	13.27		C
ANISOU	640	CD1	TYR	1230	2066	1294	1684	-115	-74	50	C
ATOM	641	CE1	TYR	1230	14.100	21.590	12.778	1.00	13.63		C
ANISOU	641	CE1	TYR	1230	2067	1133	1979	-210	-49	141	C
ATOM	642	CD2	TYR	1230	13.628	20.395	15.224	1.00	12.86		C
ANISOU	642	CD2	TYR	1230	2011	1161	1714	-25	-83	61	C
ATOM	643	CE2	TYR	1230	12.821	21.460	14.808	1.00	13.21		C
ANISOU	643	CE2	TYR	1230	2018	1314	1690	11	-273	38	C
ATOM	644	CZ	TYR	1230	13.074	22.041	13.590	1.00	13.80		C
ANISOU	644	CZ	TYR	1230	1926	1568	1750	33	-278	211	C
ATOM	645	OH	TYR	1230	12.296	23.104	13.151	1.00	15.16		O
ANISOU	645	OH	TYR	1230	2094	1770	1895	114	-195	379	O
ATOM	646	C	TYR	1230	16.296	16.434	14.294	1.00	13.45		C
ANISOU	646	C	TYR	1230	2248	1363	1500	126	148	-44	C
ATOM	647	O	TYR	1230	17.428	16.628	13.857	1.00	14.68		O
ANISOU	647	O	TYR	1230	2233	1500	1845	45	122	138	O
ATOM	648	N	ASP	1231	15.988	15.309	14.969	1.00	13.12		N

Table 1 (continued)

ANISOU	648	N	ASP	1231	2049	1322	1615	67	-14	-88	N
ATOM	649	CA	ASP	1231	16.912	14.199	15.087	1.00	12.85		C
ANISOU	649	CA	ASP	1231	1938	1356	1586	74	20	-101	C
ATOM	650	CB	ASP	1231	17.800	14.300	16.335	1.00	12.11		C
ANISOU	650	CB	ASP	1231	1649	1305	1646	-42	111	-64	C
ATOM	651	CG	ASP	1231	18.852	13.201	16.328	1.00	13.54		C
ANISOU	651	CG	ASP	1231	1656	1517	1971	59	-22	-303	C
ATOM	652	OD1	ASP	1231	18.764	12.239	15.552	1.00	15.12		O
ANISOU	652	OD1	ASP	1231	2183	1760	1801	280	21	-481	O
ATOM	653	OD2	ASP	1231	19.785	13.319	17.152	1.00	13.05		O1-
ANISOU	653	OD2	ASP	1231	1696	1605	1659	18	90	-37	O1-
ATOM	654	C	ASP	1231	16.048	12.961	15.096	1.00	12.14		C
ANISOU	654	C	ASP	1231	1766	1352	1494	96	-30	-169	C
ATOM	655	O	ASP	1231	15.519	12.559	16.128	1.00	12.72		O
ANISOU	655	O	ASP	1231	1935	1373	1526	46	11	-218	O
ATOM	656	N	LYS	1232	15.897	12.335	13.919	1.00	13.64		N
ANISOU	656	N	LYS	1232	2003	1548	1633	3	159	-325	N
ATOM	657	CA	LYS	1232	14.976	11.218	13.777	1.00	15.00		C
ANISOU	657	CA	LYS	1232	2373	1828	1498	-257	-382	-208	C
ATOM	658	CB	LYS	1232	14.963	10.750	12.305	1.00	24.66		C
ANISOU	658	CB	LYS	1232	4099	3634	1636	-1025	-286	-793	C
ATOM	659	CG	LYS	1232	16.313	10.884	11.660	1.00	37.13		C
ANISOU	659	CG	LYS	1232	5161	5661	3287	104	1519	-1586	C
ATOM	660	CD	LYS	1232	17.199	9.697	11.980	1.00	51.93		C
ANISOU	660	CD	LYS	1232	5536	7179	7014	1055	969	-916	C
ATOM	661	CE	LYS	1232	18.605	10.028	11.464	1.00	55.57		C
ANISOU	661	CE	LYS	1232	5575	7144	8395	1196	1136	406	C
ATOM	662	NZ	LYS	1232	18.593	11.387	10.827	1.00	68.08		N1+
ANISOU	662	NZ	LYS	1232	7038	8533	10294	953	146	2605	N1+
ATOM	663	C	LYS	1232	15.310	10.019	14.656	1.00	14.39		C
ANISOU	663	C	LYS	1232	2054	1359	2055	47	155	-359	C
ATOM	664	O	LYS	1232	14.401	9.225	14.897	1.00	16.41		O
ANISOU	664	O	LYS	1232	2571	1703	1960	-411	102	-364	O
ATOM	665	N	GLU	1233	16.559	9.901	15.103	1.00	14.43		N
ANISOU	665	N	GLU	1233	2151	1510	1820	341	161	-366	N
ATOM	666	CA	GLU	1233	16.941	8.733	15.897	1.00	15.23		C
ANISOU	666	CA	GLU	1233	2326	1757	1702	418	207	-380	C
ATOM	667	CB	GLU	1233	18.437	8.874	16.290	1.00	18.97		C
ANISOU	667	CB	GLU	1233	1909	2450	2847	901	527	-133	C
ATOM	668	CG	GLU	1233	18.842	7.727	17.196	1.00	26.78		C
ANISOU	668	CG	GLU	1233	3100	3308	3768	1543	-77	291	C
ATOM	669	CD	GLU	1233	20.294	7.670	17.587	1.00	30.62		C
ANISOU	669	CD	GLU	1233	3000	3794	4840	1169	-189	1158	C
ATOM	670	OE1	GLU	1233	21.067	8.508	17.036	1.00	35.64		O1-
ANISOU	670	OE1	GLU	1233	3758	3910	5874	582	-2	1131	O1-
ATOM	671	OE2	GLU	1233	20.638	6.777	18.436	1.00	30.66		O
ANISOU	671	OE2	GLU	1233	3221	3965	4464	1353	-251	918	O
ATOM	672	C	GLU	1233	16.067	8.535	17.127	1.00	15.49		C
ANISOU	672	C	GLU	1233	2147	1451	2287	521	557	-138	C
ATOM	673	O	GLU	1233	15.845	7.409	17.599	1.00	18.33		O
ANISOU	673	O	GLU	1233	3286	1388	2292	673	546	-102	O

Table 1 (continued)

ATOM	674	N	TYR	1234	15.540	9.630	17.688	1.00	12.26		N
ANISOU	674	N	TYR	1234	1826	1347	1486	374	-27	-203	N
ATOM	675	CA	TYR	1234	14.885	9.565	18.996	1.00	12.57		C
ANISOU	675	CA	TYR	1234	1769	1451	1555	157	-75	-424	C
ATOM	676	CB	TYR	1234	15.388	10.772	19.860	1.00	11.97		C
ANISOU	676	CB	TYR	1234	1811	1185	1552	69	5	-233	C
ATOM	677	CG	TYR	1234	16.871	10.571	20.112	1.00	11.31		C
ANISOU	677	CG	TYR	1234	1826	1246	1226	52	25	-229	C
ATOM	678	CD1	TYR	1234	17.857	11.285	19.432	1.00	12.23		C
ANISOU	678	CD1	TYR	1234	1874	1066	1707	40	45	-118	C
ATOM	679	CE1	TYR	1234	19.185	11.082	19.674	1.00	12.38		C
ANISOU	679	CE1	TYR	1234	1849	1262	1591	-90	-125	-278	C
ATOM	680	CD2	TYR	1234	17.286	9.625	21.060	1.00	11.77		C
ANISOU	680	CD2	TYR	1234	1788	1244	1438	-50	-99	-158	C
ATOM	681	CE2	TYR	1234	18.612	9.385	21.334	1.00	13.00		C
ANISOU	681	CE2	TYR	1234	1781	1343	1817	-56	-220	-134	C
ATOM	682	CZ	TYR	1234	19.542	10.136	20.621	1.00	12.66		C
ANISOU	682	CZ	TYR	1234	1774	1313	1722	-101	-217	-234	C
ATOM	683	OH	TYR	1234	20.878	9.923	20.871	1.00	15.18		O
ANISOU	683	OH	TYR	1234	1788	1614	2366	-255	-461	-100	O
ATOM	684	C	TYR	1234	13.374	9.508	18.919	1.00	12.83		C
ANISOU	684	C	TYR	1234	1771	1465	1639	-15	-52	-92	C
ATOM	685	O	TYR	1234	12.694	9.715	19.923	1.00	13.00		O
ANISOU	685	O	TYR	1234	1857	1492	1588	140	-37	17	O
ATOM	686	N	TYR	1235	12.821	9.202	17.720	1.00	12.60		N
ANISOU	686	N	TYR	1235	1743	1314	1729	106	-105	-279	N
ATOM	687	CA	TYR	1235	11.402	9.112	17.512	1.00	12.07		C
ANISOU	687	CA	TYR	1235	1736	1100	1748	-129	12	-294	C
ATOM	688	CB	TYR	1235	10.884	10.156	16.487	1.00	12.71		C
ANISOU	688	CB	TYR	1235	1774	1210	1846	33	-202	-321	C
ATOM	689	CG	TYR	1235	11.148	11.536	17.075	1.00	11.57		C
ANISOU	689	CG	TYR	1235	1706	1155	1537	-9	-102	-161	C
ATOM	690	CD1	TYR	1235	12.408	12.122	16.930	1.00	11.96		C
ANISOU	690	CD1	TYR	1235	1647	1172	1724	48	-92	-137	C
ATOM	691	CE1	TYR	1235	12.719	13.381	17.446	1.00	11.68		C
ANISOU	691	CE1	TYR	1235	1579	1025	1836	150	-162	-62	C
ATOM	692	CD2	TYR	1235	10.157	12.229	17.761	1.00	10.34		C
ANISOU	692	CD2	TYR	1235	1482	1062	1385	98	-356	-93	C
ATOM	693	CE2	TYR	1235	10.452	13.488	18.289	1.00	10.27		C
ANISOU	693	CE2	TYR	1235	1491	1189	1222	13	-448	-127	C
ATOM	694	CZ	TYR	1235	11.711	14.025	18.120	1.00	10.64		C
ANISOU	694	CZ	TYR	1235	1478	988	1577	120	-396	-98	C
ATOM	695	OH	TYR	1235	12.013	15.268	18.631	1.00	11.37		O
ANISOU	695	OH	TYR	1235	1391	1234	1694	-53	-285	-288	O
ATOM	696	C	TYR	1235	11.061	7.709	17.024	1.00	14.28		C
ANISOU	696	C	TYR	1235	1965	1116	2345	-38	180	-509	C
ATOM	697	O	TYR	1235	11.752	7.225	16.102	1.00	18.57		O
ANISOU	697	O	TYR	1235	2741	1768	2546	-490	578	-1034	O
ATOM	698	N	SER	1236	10.063	7.095	17.637	1.00	13.08		N
ANISOU	698	N	SER	1236	1914	1044	2010	-218	-212	-354	N
ATOM	699	CA	SER	1236	9.636	5.763	17.231	1.00	13.74		C

Table 1 (continued)

ANISOU	699	CA	SER	1236	1892	1028	2301	-34	-532	-419	C
ATOM	700	CB	SER	1236	9.928	4.783	18.376	1.00	17.45		C
ANISOU	700	CB	SER	1236	2501	1156	2974	65	-858	17	C
ATOM	701	OG	SER	1236	11.342	4.632	18.468	1.00	20.19		O
ANISOU	701	OG	SER	1236	2533	1802	3338	280	-900	-74	O
ATOM	702	C	SER	1236	8.161	5.783	16.871	1.00	13.57		C
ANISOU	702	C	SER	1236	1827	1185	2144	-74	-440	-416	C
ATOM	703	O	SER	1236	7.394	6.482	17.512	1.00	15.73		O
ANISOU	703	O	SER	1236	1899	1730	2346	34	-319	-601	O
ATOM	704	N	VAL	1237	7.810	5.006	15.850	1.00	15.64		N
ANISOU	704	N	VAL	1237	2087	1740	2113	-247	-565	-517	N
ATOM	705	CA	VAL	1237	6.430	4.956	15.390	1.00	17.22		C
ANISOU	705	CA	VAL	1237	2015	2341	2188	-262	-558	-431	C
ATOM	706	CB	VAL	1237	6.375	4.486	13.924	1.00	22.66		C
ANISOU	706	CB	VAL	1237	2719	3622	2268	-810	-709	-718	C
ATOM	707	CG1	VAL	1237	4.962	4.362	13.439	1.00	24.29		C
ANISOU	707	CG1	VAL	1237	2459	4451	2318	183	-655	-1374	C
ATOM	708	CG2	VAL	1237	7.135	5.482	13.055	1.00	26.34		C
ANISOU	708	CG2	VAL	1237	3574	3944	2488	-227	117	-196	C
ATOM	709	C	VAL	1237	5.628	4.037	16.302	1.00	17.00		C
ANISOU	709	C	VAL	1237	2126	1717	2614	-188	-419	-539	C
ATOM	710	O	VAL	1237	5.974	2.856	16.517	1.00	21.11		O
ANISOU	710	O	VAL	1237	2819	1873	3329	165	-502	-307	O
ATOM	711	N	HIS	1238	4.547	4.549	16.854	1.00	16.83		N
ANISOU	711	N	HIS	1238	2093	2136	2166	-102	-464	-478	N
ATOM	712	CA	HIS	1238	3.588	3.754	17.613	1.00	17.94		C
ANISOU	712	CA	HIS	1238	2508	2060	2250	-425	-336	-701	C
ATOM	713	CB	HIS	1238	2.644	4.602	18.465	1.00	20.86		C
ANISOU	713	CB	HIS	1238	2177	2698	3050	-584	-59	-1171	C
ATOM	714	CG	HIS	1238	1.963	3.741	19.485	1.00	23.58		C
ANISOU	714	CG	HIS	1238	2246	3890	2824	-565	-123	-785	C
ATOM	715	CD2	HIS	1238	0.865	2.951	19.298	1.00	19.89		C
ANISOU	715	CD2	HIS	1238	2255	2533	2770	-250	295	-993	C
ATOM	716	ND1	HIS	1238	2.308	3.585	20.812	1.00	30.42		N
ANISOU	716	ND1	HIS	1238	3426	5093	3039	-685	-593	-473	N
ATOM	717	CE1	HIS	1238	1.479	2.752	21.398	1.00	27.54		C
ANISOU	717	CE1	HIS	1238	3319	4300	2844	280	207	-515	C
ATOM	718	NE2	HIS	1238	0.606	2.368	20.475	1.00	27.61		N
ANISOU	718	NE2	HIS	1238	3500	3807	3183	-527	304	-313	N
ATOM	719	C	HIS	1238	2.781	2.926	16.640	1.00	19.32		C
ANISOU	719	C	HIS	1238	2881	2059	2400	-428	-761	-533	C
ATOM	720	O	HIS	1238	2.169	3.445	15.706	1.00	21.41		O
ANISOU	720	O	HIS	1238	2729	2522	2883	-383	-974	-325	O
ATOM	721	N	ASN	1239	2.792	1.606	16.882	1.00	18.74		N
ANISOU	721	N	ASN	1239	2583	2072	2465	-573	-546	-554	N
ATOM	722	CA	ASN	1239	2.197	0.775	15.812	1.00	18.67		C
ANISOU	722	CA	ASN	1239	2517	2120	2456	-305	-764	-639	C
ATOM	723	CB	ASN	1239	2.932	-0.595	15.747	1.00	22.78		C
ANISOU	723	CB	ASN	1239	3617	1967	3070	-141	29	-465	C
ATOM	724	CG	ASN	1239	2.854	-1.483	16.974	1.00	25.87		C
ANISOU	724	CG	ASN	1239	3747	2456	3625	111	-123	85	C

Table 1 (continued)

ATOM	725	OD1	ASN	1239	1.879	-1.485	17.724	1.00	26.32		O
ANISOU	725	OD1	ASN	1239	4194	2582	3224	-534	52	-132	O
ATOM	726	ND2	ASN	1239	3.939	-2.273	17.181	1.00	27.62		N
ANISOU	726	ND2	ASN	1239	4208	2441	3846	274	-1437	-934	N
ATOM	727	C	ASN	1239	0.691	0.618	15.949	1.00	23.47		C
ANISOU	727	C	ASN	1239	2573	3650	2695	-602	-666	-1115	C
ATOM	728	O	ASN	1239	0.084	-0.201	15.218	1.00	28.82		O
ANISOU	728	O	ASN	1239	2889	3944	4117	-1169	-315	-1838	O
ATOM	729	N	LYS	1240	0.045	1.375	16.824	1.00	24.60		N
ANISOU	729	N	LYS	1240	2564	3477	3306	-751	-235	-1148	N
ATOM	730	CA	LYS	1240	-1.424	1.344	16.754	1.00	25.90		C
ANISOU	730	CA	LYS	1240	2590	3777	3474	-666	-462	-1239	C
ATOM	731	CB	LYS	1240	-1.975	1.075	18.144	1.00	27.11		C
ANISOU	731	CB	LYS	1240	2595	3814	3891	-437	-23	-868	C
ATOM	736	C	LYS	1240	-1.811	2.654	16.114	1.00	27.03		C
ANISOU	736	C	LYS	1240	2832	4028	3412	-387	-319	-1091	C
ATOM	737	O	LYS	1240	-2.725	2.625	15.283	1.00	33.81		O
ANISOU	737	O	LYS	1240	2800	3811	6236	457	-1583	-1740	O
ATOM	738	N	THR	1241	-1.126	3.755	16.478	1.00	24.37		N
ANISOU	738	N	THR	1241	2705	3733	2820	-177	-308	-785	N
ATOM	739	CA	THR	1241	-1.554	5.027	15.901	1.00	23.34		C
ANISOU	739	CA	THR	1241	1883	4000	2983	49	-636	-722	C
ATOM	740	CB	THR	1241	-1.567	6.099	17.029	1.00	23.24		C
ANISOU	740	CB	THR	1241	2119	3754	2958	28	-364	-590	C
ATOM	741	OG1	THR	1241	-0.185	6.266	17.412	1.00	21.67		O
ANISOU	741	OG1	THR	1241	2081	3752	2402	419	-389	-827	O
ATOM	742	CG2	THR	1241	-2.386	5.681	18.224	1.00	27.29		C
ANISOU	742	CG2	THR	1241	2620	4356	3391	-127	166	-682	C
ATOM	743	C	THR	1241	-0.717	5.626	14.784	1.00	23.51		C
ANISOU	743	C	THR	1241	2511	3547	2875	313	-513	-703	C
ATOM	744	O	THR	1241	-1.158	6.581	14.115	1.00	24.60		O
ANISOU	744	O	THR	1241	2529	3830	2990	444	-656	-633	O
ATOM	745	N	GLY	1242	0.478	5.165	14.520	1.00	19.74		N
ANISOU	745	N	GLY	1242	2190	2967	2342	-124	-606	-528	N
ATOM	746	CA	GLY	1242	1.396	5.703	13.515	1.00	18.56		C
ANISOU	746	CA	GLY	1242	2512	2485	2054	-252	-854	-282	C
ATOM	747	C	GLY	1242	2.149	6.934	13.987	1.00	17.81		C
ANISOU	747	C	GLY	1242	2096	2277	2396	192	-975	-440	C
ATOM	748	O	GLY	1242	2.996	7.478	13.277	1.00	21.23		O
ANISOU	748	O	GLY	1242	2961	2019	3087	-156	-610	-221	O
ATOM	749	N	ALA	1243	1.871	7.430	15.207	1.00	20.71		N
ANISOU	749	N	ALA	1243	2312	2910	2645	441	-1145	-923	N
ATOM	750	CA	ALA	1243	2.493	8.659	15.691	1.00	18.68		C
ANISOU	750	CA	ALA	1243	2004	2740	2352	355	-685	-752	C
ATOM	751	CB	ALA	1243	1.851	9.097	17.001	1.00	22.28		C
ANISOU	751	CB	ALA	1243	2406	3134	2924	561	-275	-1121	C
ATOM	752	C	ALA	1243	3.989	8.481	15.904	1.00	17.19		C
ANISOU	752	C	ALA	1243	1993	2362	2178	325	-515	-190	C
ATOM	753	O	ALA	1243	4.355	7.416	16.428	1.00	16.95		O
ANISOU	753	O	ALA	1243	2233	2139	2070	220	-714	-425	O
ATOM	754	N	LYS	1244	4.830	9.446	15.543	1.00	17.19		N

Table 1 (continued)

ANISOU	754	N	LYS	1244	2226	2174	2132	173	-748	-409	N
ATOM	755	CA	LYS	1244	6.279	9.399	15.755	1.00	16.51		C
ANISOU	755	CA	LYS	1244	2242	2452	1579	-113	-561	-278	C
ATOM	756	CB	LYS	1244	6.996	10.115	14.619	1.00	24.37		C
ANISOU	756	CB	LYS	1244	3095	4447	1718	-450	-252	233	C
ATOM	761	C	LYS	1244	6.570	10.019	17.107	1.00	13.96		C
ANISOU	761	C	LYS	1244	2093	1609	1602	188	-527	-145	C
ATOM	762	O	LYS	1244	6.432	11.228	17.285	1.00	16.00		O
ANISOU	762	O	LYS	1244	2436	1569	2072	207	-586	2	O
ATOM	763	N	LEU	1245	6.966	9.237	18.106	1.00	12.09		N
ANISOU	763	N	LEU	1245	1707	1395	1491	-42	-436	-234	N
ATOM	764	CA	LEU	1245	6.978	9.680	19.503	1.00	11.64		C
ANISOU	764	CA	LEU	1245	1527	1426	1471	-70	-365	-386	C
ATOM	765	CB	LEU	1245	6.119	8.694	20.288	1.00	12.13		C
ANISOU	765	CB	LEU	1245	1376	1696	1537	48	-288	-297	C
ATOM	766	CG	LEU	1245	4.616	8.695	19.963	1.00	12.80		C
ANISOU	766	CG	LEU	1245	1394	1889	1579	40	-337	-326	C
ATOM	767	CD1	LEU	1245	3.943	7.569	20.729	1.00	16.49		C
ANISOU	767	CD1	LEU	1245	1800	2257	2209	-329	-94	-208	C
ATOM	768	CD2	LEU	1245	3.979	10.052	20.252	1.00	15.04		C
ANISOU	768	CD2	LEU	1245	1360	2084	2269	232	-539	-668	C
ATOM	769	C	LEU	1245	8.367	9.703	20.091	1.00	10.74		C
ANISOU	769	C	LEU	1245	1492	1165	1422	28	-278	-354	C
ATOM	770	O	LEU	1245	9.161	8.773	19.848	1.00	11.72		O
ANISOU	770	O	LEU	1245	1643	1174	1638	37	-155	-268	O
ATOM	771	N	PRO	1246	8.707	10.736	20.856	1.00	10.15		N
ANISOU	771	N	PRO	1246	1212	1173	1471	70	-370	-251	N
ATOM	772	CD	PRO	1246	7.886	11.940	21.084	1.00	10.19		C
ANISOU	772	CD	PRO	1246	1492	890	1490	52	-337	-168	C
ATOM	773	CA	PRO	1246	10.010	10.826	21.531	1.00	10.05		C
ANISOU	773	CA	PRO	1246	1275	959	1586	-102	-367	-74	C
ATOM	774	CB	PRO	1246	10.161	12.336	21.800	1.00	10.20		C
ANISOU	774	CB	PRO	1246	1443	968	1465	-121	-250	-20	C
ATOM	775	CG	PRO	1246	8.739	12.771	22.016	1.00	10.24		C
ANISOU	775	CG	PRO	1246	1396	863	1631	-86	-359	21	C
ATOM	776	C	PRO	1246	10.026	10.021	22.832	1.00	9.89		C
ANISOU	776	C	PRO	1246	1289	913	1555	33	-396	-103	C
ATOM	777	O	PRO	1246	10.047	10.591	23.915	1.00	9.47		O
ANISOU	777	O	PRO	1246	1217	877	1505	58	-104	-54	O
ATOM	778	N	VAL	1247	10.024	8.683	22.677	1.00	9.82		N
ANISOU	778	N	VAL	1247	1192	904	1633	-48	-359	-76	N
ATOM	779	CA	VAL	1247	9.611	7.834	23.802	1.00	10.27		C
ANISOU	779	CA	VAL	1247	1460	955	1488	-163	-351	-154	C
ATOM	780	CB	VAL	1247	9.573	6.338	23.375	1.00	12.33		C
ANISOU	780	CB	VAL	1247	1750	965	1971	-111	-538	-179	C
ATOM	781	CG1	VAL	1247	8.429	6.166	22.327	1.00	15.23		C
ANISOU	781	CG1	VAL	1247	2107	1238	2444	-242	-930	-264	C
ATOM	782	CG2	VAL	1247	10.901	5.842	22.880	1.00	13.87		C
ANISOU	782	CG2	VAL	1247	1962	1116	2193	113	-359	-333	C
ATOM	783	C	VAL	1247	10.492	8.001	25.012	1.00	9.46		C
ANISOU	783	C	VAL	1247	1157	834	1602	-90	-239	-14	C

Table 1 (continued)

ATOM	784	O	VAL	1247	9.931	7.873	26.117	1.00	10.78		O
ANISOU	784	O	VAL	1247	1355	1237	1505	-98	-236	-28	O
ATOM	785	N	ALYS	1248	11.788	8.270	24.880	0.50	9.63		N
ANISOU	785	N	ALYS	1248	1101	891	1667	133	-289	-68	N
ATOM	786	N	BLYS	1248	11.793	8.266	24.918	0.50	9.92		N
ANISOU	786	N	BLYS	1248	1149	950	1671	24	-278	-120	N
ATOM	787	CA	ALYS	1248	12.677	8.321	26.042	0.50	9.14		C
ANISOU	787	CA	ALYS	1248	1082	921	1469	47	-196	20	C
ATOM	788	CA	BLYS	1248	12.582	8.279	26.157	0.50	9.81		C
ANISOU	788	CA	BLYS	1248	1106	1029	1594	157	-256	-131	C
ATOM	789	CB	ALYS	1248	14.135	8.170	25.558	0.50	10.58		C
ANISOU	789	CB	ALYS	1248	1079	1334	1605	171	-182	-307	C
ATOM	790	CB	BLYS	1248	14.049	7.934	25.823	0.50	8.28		C
ANISOU	790	CB	BLYS	1248	1154	703	1289	94	-24	405	C
ATOM	791	CG	ALYS	1248	14.419	6.809	24.943	0.50	11.97		C
ANISOU	791	CG	ALYS	1248	1628	1363	1556	386	-310	-248	C
ATOM	792	CG	BLYS	1248	14.148	6.453	25.465	0.50	8.15		C
ANISOU	792	CG	BLYS	1248	955	625	1517	-73	116	438	C
ATOM	793	CD	ALYS	1248	14.091	5.630	25.815	0.50	21.74		C
ANISOU	793	CD	ALYS	1248	3542	1552	3168	-377	-1023	532	C
ATOM	794	CD	BLYS	1248	15.560	6.139	24.948	0.50	7.63		C
ANISOU	794	CD	BLYS	1248	725	981	1193	-81	-205	69	C
ATOM	795	CE	ALYS	1248	14.672	4.302	25.357	0.50	27.88		C
ANISOU	795	CE	ALYS	1248	5033	1399	4160	-399	-699	285	C
ATOM	796	CE	BLYS	1248	15.634	4.681	24.574	0.50	13.62		C
ANISOU	796	CE	BLYS	1248	1605	1165	2406	-106	707	-306	C
ATOM	797	NZ	ALYS	1248	15.884	4.359	24.463	0.50	23.18		N1+
ANISOU	797	NZ	ALYS	1248	6338	557	1914	-680	-709	-628	N1+
ATOM	798	NZ	BLYS	1248	15.029	4.402	23.255	0.50	31.75		N1+
ANISOU	798	NZ	BLYS	1248	7203	2562	2300	-312	72	-1528	N1+
ATOM	799	C	ALYS	1248	12.511	9.591	26.861	0.50	9.28		C
ANISOU	799	C	ALYS	1248	1189	991	1345	133	-55	14	C
ATOM	800	C	BLYS	1248	12.503	9.602	26.893	0.50	9.31		C
ANISOU	800	C	BLYS	1248	1240	937	1362	85	-117	9	C
ATOM	801	O	ALYS	1248	13.099	9.712	27.940	0.50	9.42		O
ANISOU	801	O	ALYS	1248	1099	1016	1465	107	-142	-17	O
ATOM	802	O	BLYS	1248	13.149	9.768	27.931	0.50	9.14		O
ANISOU	802	O	BLYS	1248	1037	904	1533	-1	-181	9	O
ATOM	803	N	TRP	1249	11.715	10.551	26.350	1.00	8.58		N
ANISOU	803	N	TRP	1249	1004	903	1351	47	-12	-24	N
ATOM	804	CA	TRP	1249	11.465	11.838	27.057	1.00	8.48		C
ANISOU	804	CA	TRP	1249	1030	752	1440	-181	79	-49	C
ATOM	805	CB	TRP	1249	11.708	13.061	26.125	1.00	8.69		C
ANISOU	805	CB	TRP	1249	957	974	1372	-51	-108	170	C
ATOM	806	CG	TRP	1249	13.193	13.367	26.018	1.00	7.75		C
ANISOU	806	CG	TRP	1249	957	673	1314	-22	-37	86	C
ATOM	807	CD2	TRP	1249	14.147	12.647	25.209	1.00	8.70		C
ANISOU	807	CD2	TRP	1249	1083	879	1345	67	-135	-9	C
ATOM	808	CE2	TRP	1249	15.402	13.266	25.414	1.00	8.28		C
ANISOU	808	CE2	TRP	1249	987	772	1387	53	-121	65	C
ATOM	809	CE3	TRP	1249	14.074	11.544	24.333	1.00	8.54		C

Table 1 (continued)

ANISOU	809	CE3	TRP	1249	1124	984	1139	152	-232	-74	C
ATOM	810	CD1	TRP	1249	13.873	14.357	26.653	1.00	7.93		C
ANISOU	810	CD1	TRP	1249	953	798	1264	-45	-95	110	C
ATOM	811	NE1	TRP	1249	15.199	14.305	26.300	1.00	8.43		N
ANISOU	811	NE1	TRP	1249	945	966	1292	40	-115	-47	N
ATOM	812	CZ2	TRP	1249	16.593	12.854	24.803	1.00	9.43		C
ANISOU	812	CZ2	TRP	1249	1161	1024	1398	213	-128	-14	C
ATOM	813	CZ3	TRP	1249	15.265	11.145	23.735	1.00	9.35		C
ANISOU	813	CZ3	TRP	1249	1172	1021	1358	-3	23	48	C
ATOM	814	CH2	TRP	1249	16.492	11.769	23.952	1.00	8.87		C
ANISOU	814	CH2	TRP	1249	1243	887	1240	-34	-48	92	C
ATOM	815	C	TRP	1249	10.052	11.867	27.576	1.00	8.29		C
ANISOU	815	C	TRP	1249	928	880	1340	-130	-91	-189	C
ATOM	816	O	TRP	1249	9.658	12.790	28.276	1.00	9.05		O
ANISOU	816	O	TRP	1249	1129	964	1347	-116	14	-184	O
ATOM	817	N	MET	1250	9.213	10.862	27.244	1.00	8.66		N
ANISOU	817	N	MET	1250	921	961	1406	-146	-220	-41	N
ATOM	818	CA	MET	1250	7.778	10.926	27.573	1.00	8.65		C
ANISOU	818	CA	MET	1250	881	997	1409	-142	-90	-110	C
ATOM	819	CB	MET	1250	7.015	10.063	26.551	1.00	9.17		C
ANISOU	819	CB	MET	1250	1047	965	1472	-73	-217	-93	C
ATOM	820	CO	MET	1250	6.915	10.787	25.213	1.00	9.81		C
ANISOU	820	CG	MET	1250	1272	1034	1419	-31	-212	-106	C
ATOM	821	SD	MET	1250	6.299	9.746	23.864	1.00	11.09		S
ANISOU	821	SD	MET	1250	1384	1297	1532	-47	-241	-180	S
ATOM	822	CE	MET	1250	4.668	9.277	24.509	1.00	13.16		C
ANISOU	822	CE	MET	1250	1122	1553	2324	-68	-312	-187	C
ATOM	823	C	MET	1250	7.460	10.447	28.954	1.00	8.39		C
ANISOU	823	C	MET	1250	912	836	1439	-144	-200	-102	C
ATOM	824	O	MET	1250	8.046	9.519	29.537	1.00	9.38		O
ANISOU	824	O	MET	1250	925	1087	1552	-4	-115	49	O
ATOM	825	N	ALA	1251	6.438	11.094	29.531	1.00	8.78		N
ANISOU	825	N	ALA	1251	1069	892	1376	-176	-61	-153	N
ATOM	826	CA	ALA	1251	5.923	10.619	30.811	1.00	8.54		C
ANISOU	826	CA	ALA	1251	1053	802	1391	-26	-140	-36	C
ATOM	827	CB	ALA	1251	4.892	11.612	31.359	1.00	9.51		C
ANISOU	827	CB	ALA	1251	1141	782	1690	-103	119	-59	C
ATOM	828	C	ALA	1251	5.286	9.262	30.688	1.00	8.58		C
ANISOU	828	C	ALA	1251	968	768	1524	26	-184	4	C
ATOM	829	O	ALA	1251	4.736	8.885	29.620	1.00	9.32		O
ANISOU	829	O	ALA	1251	1077	919	1547	-78	-152	-37	O
ATOM	830	N	LEU	1252	5.296	8.482	31.771	1.00	9.16		N
ANISOU	830	N	LEU	1252	1016	908	1558	-96	-109	48	N
ATOM	831	CA	LEU	1252	4.687	7.155	31.775	1.00	10.01		C
ANISOU	831	CA	LEU	1252	1071	922	1812	-131	-31	143	C
ATOM	832	CB	LEU	1252	4.776	6.596	33.208	1.00	12.06		C
ANISOU	832	CB	LEU	1252	1405	1239	1940	-242	-154	351	C
ATOM	833	CG	LEU	1252	3.998	5.268	33.395	1.00	13.40		C
ANISOU	833	CG	LEU	1252	2008	1121	1962	-385	-196	278	C
ATOM	834	CD1	LEU	1252	4.521	4.208	32.441	1.00	14.50		C
ANISOU	834	CD1	LEU	1252	1388	1196	2926	10	64	180	C

Table 1 (continued)

ATOM	835	CD2	LEU	1252	4.067	4.880	34.868	1.00	19.82		C
ANISOU	835	CD2	LEU	1252	3335	1959	2236	-591	-259	871	C
ATOM	836	C	LEU	1252	3.264	7.225	31.270	1.00	10.09		C
ANISOU	836	C	LEU	1252	1084	940	1810	-211	-75	14	C
ATOM	837	O	LEU	1252	2.882	6.401	30.412	1.00	11.71		O
ANISOU	837	O	LEU	1252	1402	1028	2021	-177	-179	-164	O
ATOM	838	N	GLU	1253	2.461	8.184	31.764	1.00	10.22		N
ANISOU	838	N	GLU	1253	1098	1072	1713	-70	-80	73	N
ATOM	839	CA	GLU	1253	1.062	8.178	31.285	1.00	10.56		C
ANISOU	839	CA	GLU	1253	1015	1191	1804	-192	-79	-87	C
ATOM	840	CB	GLU	1253	0.201	9.137	32.127	1.00	10.89		C
ANISOU	840	CB	GLU	1253	1176	952	2011	-34	-217	-164	C
ATOM	841	CG	GLU	1253	0.474	10.637	31.937	1.00	11.20		C
ANISOU	841	CG	GLU	1253	1042	1050	2166	-305	-334	101	C
ATOM	842	CD	GLU	1253	1.617	11.161	32.766	1.00	10.23		C
ANISOU	842	CD	GLU	1253	970	1027	1891	-39	-267	8	C
ATOM	843	OE1	GLU	1253	2.374	10.378	33.400	1.00	9.77		O1-
ANISOU	843	OE1	GLU	1253	1080	977	1656	-10	-226	-123	O1-
ATOM	844	OE2	GLU	1253	1.769	12.415	32.774	1.00	9.75		O
ANISOU	844	OE2	GLU	1253	1054	1036	1617	-9	-345	-46	O
ATOM	845	C	GLU	1253	0.981	8.473	29.784	1.00	10.97		C
ANISOU	845	C	GLU	1253	1117	1195	1855	-123	-206	-28	C
ATOM	846	O	GLU	1253	0.063	7.923	29.125	1.00	13.27		O
ANISOU	846	O	GLU	1253	1399	1701	1943	-518	-290	39	O
ATOM	847	N	SER	1254	1.850	9.287	29.221	1.00	10.26		N
ANISOU	847	N	SER	1254	1237	991	1672	-143	-257	-69	N
ATOM	848	CA	SER	1254	1.807	9.558	27.789	1.00	10.71		C
ANISOU	848	CA	SER	1254	1341	1005	1724	-59	-280	-44	C
ATOM	849	CB	SER	1254	2.744	10.707	27.417	1.00	10.39		C
ANISOU	849	CB	SER	1254	1341	980	1627	-103	-176	-156	C
ATOM	850	OG	SER	1254	2.429	11.869	28.160	1.00	10.02		O
ANISOU	850	OG	SER	1254	1180	1045	1582	37	-205	-149	O
ATOM	851	C	SER	1254	2.207	8.343	26.984	1.00	10.47		C
ANISOU	851	C	SER	1254	1159	1045	1773	-43	-326	-131	C
ATOM	852	O	SER	1254	1.714	8.104	25.867	1.00	11.49		O
ANISOU	852	O	SER	1254	1533	1155	1678	-37	-322	-78	O
ATOM	853	N	LEU	1255	3.142	7.531	27.514	1.00	10.60		N
ANISOU	853	N	LEU	1255	1348	984	1694	-16	-328	-168	N
ATOM	854	CA	LEU	1255	3.426	6.252	26.846	1.00	11.75		C
ANISOU	854	CA	LEU	1255	1418	872	2173	-4	-392	-191	C
ATOM	855	CB	LEU	1255	4.612	5.589	27.552	1.00	11.19		C
ANISOU	855	CB	LEU	1255	1396	946	1910	-103	-333	-85	C
ATOM	856	CG	LEU	1255	5.949	6.310	27.337	1.00	11.29		C
ANISOU	856	CG	LEU	1255	1349	1000	1940	-75	-146	13	C
ATOM	857	CD1	LEU	1255	6.924	5.851	28.433	1.00	13.05		C
ANISOU	857	CD1	LEU	1255	1529	1118	2311	-99	-479	-71	C
ATOM	858	CD2	LEU	1255	6.512	6.078	25.958	1.00	13.40		C
ANISOU	858	CD2	LEU	1255	1525	1468	2098	83	-34	-183	C
ATOM	859	C	LEU	1255	2.217	5.357	26.847	1.00	11.82		C
ANISOU	859	C	LEU	1255	1463	1052	1974	-104	-428	-175	C
ATOM	860	O	LEU	1255	2.002	4.562	25.902	1.00	16.25		O

Table 1 (continued)

ANISOU	860	O	LEU	1255	2075	1654	2445	-310	-339	-736	O
ATOM	861	N	GLN	1256	1.379	5.441	27.868	1.00	12.35		N
ANISOU	861	N	GLN	1256	1400	1097	2195	-177	-339	-212	N
ATOM	862	CA	GLN	1256	0.241	4.536	27.950	1.00	14.25		C
ANISOU	862	CA	GLN	1256	1413	1306	2695	-287	-429	49	C
ATOM	863	CB	GLN	1256	-0.158	4.360	29.406	1.00	15.54		C
ANISOU	863	CB	GLN	1256	1577	1638	2689	-420	-360	130	C
ATOM	864	CG	GLN	1256	0.898	3.595	30.211	1.00	17.67		C
ANISOU	864	CG	GLN	1256	1628	2052	3032	-488	-434	550	C
ATOM	865	CD	GLN	1256	0.579	3.640	31.702	1.00	25.26		C
ANISOU	865	CD	GLN	1256	3689	2920	2989	236	-247	1030	C
ATOM	866	OE1	GLN	1256	0.571	2.651	32.409	1.00	33.40		O
ANISOU	866	OE1	GLN	1256	5253	3444	3991	371	457	1764	O
ATOM	867	NE2	GLN	1256	0.274	4.834	32.270	1.00	20.31		N
ANISOU	867	NE2	GLN	1256	2108	2958	2653	-988	-268	488	N
ATOM	868	C	GLN	1256	-0.979	5.040	27.162	1.00	14.41		C
ANISOU	868	C	GLN	1256	1496	1276	2704	-221	-565	-290	C
ATOM	869	O	GLN	1256	-1.744	4.212	26.666	1.00	19.15		O
ANISOU	869	O	GLN	1256	1968	1471	3839	-449	-1153	-302	O
ATOM	870	N	THR	1257	-1.161	6.367	27.054	1.00	13.58		N
ANISOU	870	N	THR	1257	1400	1266	2493	-202	-545	-226	N
ATOM	871	CA	THR	1257	-2.367	6.945	26.491	1.00	13.00		C
ANISOU	871	CA	THR	1257	1102	1487	2350	-205	-258	-199	C
ATOM	872	CB	THR	1257	-3.095	7.860	27.520	1.00	14.02		C
ANISOU	872	CB	THR	1257	1477	1687	2164	-192	-263	-287	C
ATOM	873	OG1	THR	1257	-2.289	9.015	27.788	1.00	15.04		O
ANISOU	873	OG1	THR	1257	1625	1493	2599	-61	-332	-289	O
ATOM	874	CG2	THR	1257	-3.328	7.100	28.825	1.00	17.43		C
ANISOU	874	CG2	THR	1257	1797	2560	2265	-614	-154	-53	C
ATOM	875	C	THR	1257	-2.121	7.799	25.260	1.00	12.77		C
ANISOU	875	C	THR	1257	1453	1369	2029	-169	-389	-452	C
ATOM	876	O	THR	1257	-3.102	8.153	24.589	1.00	14.50		O
ANISOU	876	O	THR	1257	1622	1472	2415	14	-567	-386	O
ATOM	877	N	GLN	1258	-0.866	8.123	24.996	1.00	12.61		N
ANISOU	877	N	GLN	1258	1460	1390	1940	-295	-206	-461	N
ATOM	878	CA	GLN	1258	-0.475	9.058	23.933	1.00	13.06		C
ANISOU	878	CA	GLN	1258	1506	1582	1874	34	-302	-327	C
ATOM	879	CB	GLN	1258	-0.763	8.510	22.508	1.00	15.10		C
ANISOU	879	CB	GLN	1258	2218	1586	1934	247	-720	-361	C
ATOM	880	CG	GLN	1258	0.195	7.368	22.136	1.00	27.52		C
ANISOU	880	CG	GLN	1258	4054	3442	2959	1580	-257	-1265	C
ATOM	881	CD	GLN	1258	0.030	6.833	20.720	1.00	29.05		C
ANISOU	881	CD	GLN	1258	4243	3526	3268	575	167	-1667	C
ATOM	882	OE1	GLN	1258	0.056	7.547	19.703	1.00	29.12		O
ANISOU	882	OE1	GLN	1258	2551	5558	2956	338	-369	-1137	O
ATOM	883	NE2	GLN	1258	-0.144	5.520	20.642	1.00	50.54		N
ANISOU	883	NE2	GLN	1258	9112	3861	6229	-732	-858	-2302	N
ATOM	884	C	GLN	1258	-1.111	10.436	24.128	1.00	12.97		C
ANISOU	884	C	GLN	1258	1335	1540	2053	38	-421	-330	C
ATOM	885	O	GLN	1258	-1.295	11.139	23.139	1.00	17.50		O
ANISOU	885	O	GLN	1258	2771	1703	2175	332	-305	-211	O

Table 1 (continued)

ATOM	886	N	LYS	1259	-1.399	10.818	25.358	1.00	12.05		N
ANISOU	886	N	LYS	1259	1110	1372	2096	-30	-432	-361	N
ATOM	887	CA	LYS	1259	-1.856	12.156	25.682	1.00	13.46		C
ANISOU	887	CA	LYS	1259	1412	1410	2290	-81	-500	-552	C
ATOM	888	CB	LYS	1259	-3.134	12.102	26.533	1.00	13.68		C
ANISOU	888	CB	LYS	1259	1378	1409	2413	7	-435	-561	C
ATOM	889	CG	LYS	1259	-4.299	11.378	25.839	1.00	17.48		C
ANISOU	889	CG	LYS	1259	1572	1747	3323	-424	-570	-618	C
ATOM	890	CD	LYS	1259	-5.560	11.502	26.639	1.00	27.58		C
ANISOU	890	CD	LYS	1259	1733	3758	4986	-613	57	-489	C
ATOM	891	CE	LYS	1259	-5.581	10.720	27.941	1.00	39.60		C
ANISOU	891	CE	LYS	1259	4356	4331	6358	-482	2233	823	C
ATOM	892	NZ	LYS	1259	-6.900	10.847	28.634	1.00	55.65		N1+
ANISOU	892	NZ	LYS	1259	6166	7166	7811	-848	4140	-1006	N1+
ATOM	893	C	LYS	1259	-0.788	12.950	26.438	1.00	10.47		C
ANISOU	893	C	LYS	1259	1208	1064	1706	104	-423	-121	C
ATOM	894	O	LYS	1259	-0.118	12.374	27.302	1.00	12.68		O
ANISOU	894	O	LYS	1259	1335	1228	2256	-10	-523	233	O
ATOM	895	N	PHE	1260	-0.652	14.221	26.105	1.00	9.90		N
ANISOU	895	N	PHE	1260	1071	1101	1590	61	-293	-118	N
ATOM	896	CA	PHE	1260	0.368	15.094	26.671	1.00	9.35		C
ANISOU	896	CA	PHE	1260	846	1223	1482	-10	-226	-65	C
ATOM	897	CB	PHE	1260	1.205	15.610	25.518	1.00	9.78		C
ANISOU	897	CB	PHE	1260	1015	1258	1444	239	-100	100	C
ATOM	898	CG	PHE	1260	2.037	14.570	24.764	1.00	9.93		C
ANISOU	898	CG	PHE	1260	1091	1189	1493	117	-131	30	C
ATOM	899	CD1	PHE	1260	1.426	13.739	23.827	1.00	12.20		C
ANISOU	899	CD1	PHE	1260	1442	1429	1763	-47	-31	-248	C
ATOM	900	CD2	PHE	1260	3.403	14.445	25.016	1.00	9.98		C
ANISOU	900	CD2	PHE	1260	1030	1132	1629	290	7	199	C
ATOM	901	CE1	PHE	1260	2.185	12.787	23.150	1.00	12.36		C
ANISOU	901	CE1	PHE	1260	1117	2008	1569	148	-134	-387	C
ATOM	902	CE2	PHE	1260	4.145	13.515	24.317	1.00	9.86		C
ANISOU	902	CE2	PHE	1260	1131	998	1618	52	-106	-70	C
ATOM	903	CZ	PHE	1260	3.547	12.668	23.357	1.00	11.24		C
ANISOU	903	CZ	PHE	1260	1120	1418	1733	-165	-259	-42	C
ATOM	904	C	PHE	1260	-0.225	16.264	27.418	1.00	9.28		C
ANISOU	904	C	PHE	1260	871	1209	1447	-47	-157	-64	C
ATOM	905	O	PHE	1260	-1.337	16.736	27.026	1.00	10.47		O
ANISOU	905	O	PHE	1260	924	1259	1793	40	-303	-96	O
ATOM	906	N	THR	1261	0.443	16.749	28.454	1.00	9.04		N
ANISOU	906	N	THR	1261	1043	909	1482	-23	-249	20	N
ATOM	907	CA	THR	1261	-0.016	17.823	29.305	1.00	8.91		C
ANISOU	907	CA	THR	1261	942	1087	1357	-35	-77	13	C
ATOM	908	CB	THR	1261	-0.725	17.340	30.585	1.00	9.86		C
ANISOU	908	CB	THR	1261	989	1226	1531	-57	-116	240	C
ATOM	909	OG1	THR	1261	0.289	16.658	31.382	1.00	9.74		O
ANISOU	909	OG1	THR	1261	993	1265	1441	-60	-226	120	O
ATOM	910	CG2	THR	1261	-1.887	16.398	30.267	1.00	10.68		C
ANISOU	910	CG2	THR	1261	838	1633	1588	-132	-151	173	C
ATOM	911	C	THR	1261	1.182	18.639	29.764	1.00	7.61		C

Table 1 (continued)

ANISOU	911	C	THR	1261	817	841	1233	144	-203	165	C
ATOM	912	O	THR	1261	2.349	18.273	29.550	1.00	8.44		O
ANISOU	912	O	THR	1261	838	968	1400	24	-121	21	O
ATOM	913	N	THR	1262	0.909	19.760	30.453	1.00	8.82		N
ANISOU	913	N	THR	1262	1028	949	1374	106	-117	28	N
ATOM	914	CA	THR	1262	2.019	20.496	31.050	1.00	9.61		C
ANISOU	914	CA	THR	1262	1246	1075	1332	136	-216	-52	C
ATOM	915	CB	THR	1262	1.514	21.803	31.709	1.00	10.84		C
ANISOU	915	CB	THR	1262	1416	1102	1600	280	27	-244	C
ATOM	916	OG1	THR	1262	1.244	22.765	30.710	1.00	15.47		O
ANISOU	916	OG1	THR	1262	2206	1297	2374	325	441	180	O
ATOM	917	CG2	THR	1262	2.583	22.456	32.507	1.00	13.18		C
ANISOU	917	CG2	THR	1262	1070	1106	2831	-219	400	-612	C
ATOM	918	C	THR	1262	2.759	19.604	32.050	1.00	8.07		C
ANISOU	918	C	THR	1262	897	905	1262	-41	-28	43	C
ATOM	919	O	THR	1262	3.977	19.743	32.175	1.00	8.72		O
ANISOU	919	O	THR	1262	1046	951	1317	-130	-169	73	O
ATOM	920	N	LYS	1263	2.094	18.698	32.767	1.00	8.94		N
ANISOU	920	N	LYS	1263	985	858	1553	45	0	98	N
ATOM	921	CA	LYS	1263	2.813	17.825	33.712	1.00	8.70		C
ANISOU	921	CA	LYS	1263	982	908	1416	104	43	96	C
ATOM	922	CB	LYS	1263	1.832	17.135	34.678	1.00	10.07		C
ANISOU	922	CB	LYS	1263	1076	1477	1275	96	96	145	C
ATOM	923	CG	LYS	1263	1.227	18.072	35.713	1.00	10.66		C
ANISOU	923	CG	LYS	1263	1224	1377	1448	237	79	99	C
ATOM	924	CD	LYS	1263	2.288	18.805	36.545	1.00	11.75		C
ANISOU	924	CD	LYS	1263	1599	1241	1624	181	6	9	C
ATOM	925	CE	LYS	1263	1.583	19.329	37.814	1.00	13.94		C
ANISOU	925	CE	LYS	1263	1812	1617	1869	-43	217	-304	C
ATOM	926	NZ	LYS	1263	2.476	20.303	38.497	1.00	14.77		N1+
ANISOU	926	NZ	LYS	1263	1949	1712	1952	359	-493	-284	N1+
ATOM	927	C	LYS	1263	3.645	16.782	32.960	1.00	8.04		C
ANISOU	927	C	LYS	1263	876	835	1342	65	-42	70	C
ATOM	928	O	LYS	1263	4.644	16.330	33.528	1.00	8.67		O
ANISOU	928	O	LYS	1263	843	851	1600	-18	-154	90	O
ATOM	929	N	SER	1264	3.285	16.377	31.730	1.00	8.43		N
ANISOU	929	N	SER	1264	1062	820	1322	35	-54	110	N
ATOM	930	CA	SER	1264	4.239	15.520	31.006	1.00	8.11		C
ANISOU	930	CA	SER	1264	892	900	1288	-134	-31	10	C
ATOM	931	CB	SER	1264	3.545	14.650	29.938	1.00	8.33		C
ANISOU	931	CB	SER	1264	977	883	1305	-55	-189	29	C
ATOM	932	OG	SER	1264	2.862	15.382	28.920	1.00	8.85		O
ANISOU	932	OG	SER	1264	941	936	1486	87	-185	-29	O
ATOM	933	C	SER	1264	5.386	16.367	30.451	1.00	7.34		C
ANISOU	933	C	SER	1264	816	797	1176	45	-216	122	C
ATOM	934	O	SER	1264	6.478	15.830	30.253	1.00	8.07		O
ANISOU	934	O	SER	1264	777	930	1358	93	-147	-61	O
ATOM	935	N	ASP	1265	5.201	17.695	30.212	1.00	7.88		N
ANISOU	935	N	ASP	1265	818	733	1441	-20	-55	56	N
ATOM	936	CA	ASP	1265	6.348	18.545	29.911	1.00	7.40		C
ANISOU	936	CA	ASP	1265	844	754	1214	-67	-221	20	C

Table 1 (continued)

ATOM	937	CB	ASP	1265	5.925	19.972	29.593	1.00	8.17		C
ANISOU	937	CB	ASP	1265	946	802	1356	-47	-329	154	C
ATOM	938	CG	ASP	1265	5.376	20.206	28.183	1.00	7.76		C
ANISOU	938	CG	ASP	1265	774	897	1276	71	-65	161	C
ATOM	939	OD1	ASP	1265	5.492	19.321	27.291	1.00	7.98		O
ANISOU	939	OD1	ASP	1265	870	958	1203	-115	-99	38	O
ATOM	940	OD2	ASP	1265	4.841	21.320	27.975	1.00	8.32		O1-
ANISOU	940	OD2	ASP	1265	958	892	1311	77	-163	188	O1-
ATOM	941	C	ASP	1265	7.299	18.585	31.103	1.00	6.76		C
ANISOU	941	C	ASP	1265	746	647	1174	129	-82	-42	C
ATOM	942	O	ASP	1265	8.520	18.634	30.897	1.00	7.39		O
ANISOU	942	O	ASP	1265	749	916	1144	54	-79	2	O
ATOM	943	N	VAL	1266	6.753	18.579	32.336	1.00	7.24		N
ANISOU	943	N	VAL	1266	904	721	1124	25	-16	46	N
ATOM	944	CA	VAL	1266	7.633	18.521	33.526	1.00	7.58		C
ANISOU	944	CA	VAL	1266	886	831	1160	201	-39	-33	C
ATOM	945	CB	VAL	1266	6.784	18.670	34.809	1.00	7.71		C
ANISOU	945	CB	VAL	1266	955	838	1136	178	-55	-7	C
ATOM	946	CG1	VAL	1266	7.629	18.366	36.036	1.00	8.14		C
ANISOU	946	CG1	VAL	1266	999	958	1135	140	-84	-59	C
ATOM	947	CG2	VAL	1266	6.170	20.085	34.890	1.00	8.87		C
ANISOU	947	CG2	VAL	1266	1004	919	1447	314	22	-114	C
ATOM	948	C	VAL	1266	8.458	17.268	33.523	1.00	7.30		C
ANISOU	948	C	VAL	1266	788	781	1207	45	-120	-86	C
ATOM	949	O	VAL	1266	9.671	17.313	33.812	1.00	7.44		O
ANISOU	949	O	VAL	1266	711	864	1252	48	-95	12	O
ATOM	950	N	TRP	1267	7.853	16.108	33.200	1.00	7.36		N
ANISOU	950	N	TRP	1267	799	706	1291	-35	28	101	N
ATOM	951	CA	TRP	1267	8.630	14.883	33.089	1.00	7.73		C
ANISOU	951	CA	TRP	1267	967	731	1238	-62	68	-181	C
ATOM	952	CB	TRP	1267	7.673	13.725	32.643	1.00	8.01		C
ANISOU	952	CB	TRP	1267	832	780	1431	-71	-137	-29	C
ATOM	953	CG	TRP	1267	8.413	12.393	32.544	1.00	7.77		C
ANISOU	953	CG	TRP	1267	899	699	1356	-70	-125	2	C
ATOM	954	CD2	TRP	1267	8.136	11.215	33.337	1.00	8.17		C
ANISOU	954	CD2	TRP	1267	813	854	1439	-75	-191	53	C
ATOM	955	CE2	TRP	1267	9.045	10.219	32.923	1.00	7.97		C
ATOM	956	CE3	TRP	1267	7.217	10.914	34.336	1.00	8.27		C
ANISOU	956	CE3	TRP	1267	1093	793	1256	-282	-154	-40	C
ATOM	957	CD1	TRP	1267	9.450	11.997	31.730	1.00	7.98		C
ANISOU	957	CD1	TRP	1267	851	741	1439	-53	-136	-21	C
ATOM	958	NE1	TRP	1267	9.835	10.749	31.944	1.00	8.02		N
ANISOU	958	NE1	TRP	1267	1153	583	1311	-19	-153	-16	N
ATOM	959	CZ2	TRP	1267	9.066	8.931	33.488	1.00	9.37		C
ANISOU	959	CZ2	TRP	1267	1231	792	1539	-133	-285	120	C
ATOM	960	CZ3	TRP	1267	7.220	9.645	34.904	1.00	9.43		C
ANISOU	960	CZ3	TRP	1267	1135	868	1582	-195	-352	128	C
ATOM	961	CH2	TRP	1267	8.147	8.658	34.471	1.00	9.55		C
ANISOU	961	CH2	TRP	1267	1061	931	1635	-162	-290	147	C
ATOM	962	C	TRP	1267	9.788	15.067	32.135	1.00	7.32		C
ANISOU	962	C	TRP	1267	739	753	1291	-18	-76	25	C

Table 1 (continued)

ATOM	963	O	TRP	1267	10.953	14.743	32.421	1.00	7.52		O
ANISOU	963	O	TRP	1267	807	744	1306	58	-86	18	O
ATOM	964	N	SER	1268	9.488	15.533	30.906	1.00	7.16		N
ANISOU	964	N	SER	1268	836	704	1180	-59	-59	-99	N
ATOM	965	CA	SER	1268	10.514	15.718	29.883	1.00	7.21		C
ANISOU	965	CA	SER	1268	814	943	983	-96	-157	-158	C
ATOM	966	CB	SER	1268	9.934	16.279	28.588	1.00	8.08		C
ANISOU	966	CB	SER	1268	940	1030	1100	-32	-288	-132	C
ATOM	967	OG	SER	1268	8.923	15.395	28.105	1.00	8.68		O
ANISOU	967	OG	SER	1268	933	1281	1083	-106	-185	-291	O
ATOM	968	C	SER	1268	11.598	16.669	30.373	1.00	6.52		C
ANISOU	968	C	SER	1268	775	747	955	-60	-99	-25	C
ATOM	969	O	SER	1268	12.760	16.452	30.090	1.00	7.61		O
ANISOU	969	O	SER	1268	729	890	1273	-16	-93	-55	O
ATOM	970	N	PHE	1269	11.204	17.719	31.093	1.00	7.11		N
ANISOU	970	N	PHE	1269	928	738	1036	-63	-114	-59	N
ATOM	971	CA	PHE	1269	12.197	18.622	31.664	1.00	7.37		C
ANISOU	971	CA	PHE	1269	912	796	1091	-38	-181	-96	C
ATOM	972	CB	PHE	1269	11.443	19.747	32.412	1.00	7.74		C
ANISOU	972	CB	PHE	1269	908	674	1359	11	-131	-131	C
ATOM	973	CG	PHE	1269	12.443	20.664	33.096	1.00	7.06		C
ANISOU	973	CG	PHE	1269	727	735	1222	90	-116	-48	C
ATOM	974	CD1	PHE	1269	13.211	21.577	32.359	1.00	8.64		C
ANISOU	974	CD1	PHE	1269	1030	794	1459	-123	-45	-94	C
ATOM	975	CD2	PHE	1269	12.635	20.611	34.465	1.00	8.40		C
ANISOU	975	CD2	PHE	1269	1050	926	1216	-10	-115	-222	C
ATOM	976	CE1	PHE	1269	14.147	22.417	32.983	1.00	8.28		C
ANISOU	976	CE1	PHE	1269	871	882	1394	0	-82	-117	C
ATOM	977	CE2	PHE	1269	13.546	21.435	35.071	1.00	9.50		C
ANISOU	977	CE2	PHE	1269	1144	1048	1417	-234	-251	-38	C
ATOM	978	CZ	PHE	1269	14.313	22.316	34.363	1.00	8.75		C
ANISOU	978	CZ	PHE	1269	1129	863	1332	-29	-81	-71	C
ATOM	979	C	PHE	1269	13.143	17.892	32.575	1.00	6.90		C
ANISOU	979	C	PHE	1269	703	771	1148	41	8	-57	C
ATOM	980	O	PHE	1269	14.345	18.158	32.565	1.00	7.15		O
ANISOU	980	O	PHE	1269	776	764	1178	27	-34	-100	O
ATOM	981	N	GLY	1270	12.657	16.947	33.403	1.00	7.57		N
ANISOU	981	N	GLY	1270	1118	633	1126	-8	-144	-83	N
ATOM	982	CA	GLY	1270	13.594	16.170	34.225	1.00	7.83		C
ANISOU	982	CA	GLY	1270	962	772	1241	156	0	-12	C
ATOM	983	C	GLY	1270	14.597	15.408	33.386	1.00	7.57		C
ANISOU	983	C	GLY	1270	913	789	1174	29	-29	-36	C
ATOM	984	O	GLY	1270	15.776	15.324	33.736	1.00	7.73		O
ANISOU	984	O	GLY	1270	917	887	1133	84	-108	40	O
ATOM	985	N	VAL	1271	14.126	14.821	32.251	1.00	7.23		N
ANISOU	985	N	VAL	1271	818	715	1215	-31	38	-55	N
ATOM	986	CA	VAL	1271	15.097	14.135	31.367	1.00	7.44		C
ANISOU	986	CA	VAL	1271	927	778	1123	-35	5	-7	C
ATOM	987	CB	VAL	1271	14.351	13.356	30.259	1.00	7.77		C
ANISOU	987	CB	VAL	1271	1007	896	1050	-119	33	-43	C
ATOM	988	CG1	VAL	1271	15.389	12.624	29.387	1.00	8.65		C

Table 1 (continued)

ANISOU	988	CG1	VAL	1271	997	1157	1131	93	-62	-99	C
ATOM	989	CG2	VAL	1271	13.332	12.384	30.846	1.00	8.36		C
ANISOU	989	CG2	VAL	1271	1066	729	1381	-76	51	43	C
ATOM	990	C	VAL	1271	16.087	15.131	30.795	1.00	6.88		C
ANISOU	990	C	VAL	1271	806	703	1104	13	52	-66	C
ATOM	991	O	VAL	1271	17.268	14.845	30.710	1.00	7.71		O
ANISOU	991	O	VAL	1271	824	805	1302	46	-69	-83	O
ATOM	992	N	LEU	1272	15.620	16.326	30.397	1.00	7.21		N
ANISOU	992	N	LEU	1272	940	683	1119	-85	-32	39	N
ATOM	993	CA	LEU	1272	16.534	17.350	29.901	1.00	7.04		C
ANISOU	993	CA	LEU	1272	838	621	1216	-81	-184	8	C
ATOM	994	CB	LEU	1272	15.653	18.556	29.495	1.00	7.68		C
ANISOU	994	CB	LEU	1272	857	783	1279	58	-68	198	C
ATOM	995	CG	LEU	1272	16.433	19.702	28.801	1.00	8.64		C
ANISOU	995	CG	LEU	1272	994	782	1508	-9	-92	256	C
ATOM	996	CD1	LEU	1272	15.489	20.459	27.866	1.00	9.57		C
ANISOU	996	CD1	LEU	1272	1351	990	1297	219	-203	185	C
ATOM	997	CD2	LEU	1272	17.031	20.708	29.753	1.00	11.08		C
ANISOU	997	CD2	LEU	1272	1282	1065	1863	-304	-528	365	C
ATOM	998	C	LEU	1272	17.568	17.706	30.939	1.00	7.19		C
ANISOU	998	C	LEU	1272	772	835	1126	56	-36	-145	C
ATOM	999	O	LEU	1272	18.756	17.884	30.611	1.00	7.61		O
ANISOU	999	O	LEU	1272	745	863	1281	59	-51	77	O
ATOM	1000	N	LEU	1273	17.180	17.808	32.230	1.00	8.06		N
ANISOU	1000	N	LEU	1273	1018	966	1080	-54	-68	-115	N
ATOM	1001	CA	LEU	1273	18.221	18.053	33.239	1.00	7.63		C
ANISOU	1001	CA	LEU	1273	882	940	1076	-14	-36	34	C
ATOM	1002	CB	LEU	1273	17.571	18.155	34.654	1.00	8.61		C
ANISOU	1002	CB	LEU	1273	1131	1003	1137	37	40	-11	C
ATOM	1003	CG	LEU	1273	16.765	19.385	34.970	1.00	8.37		C
ANISOU	1003	CG	LEU	1273	902	1042	1236	-24	7	-97	C
ATOM	1004	CD1	LEU	1273	16.153	19.237	36.370	1.00	10.51		C
ANISOU	1004	CD1	LEU	1273	1428	1265	1301	168	245	173	C
ATOM	1005	CD2	LEU	1273	17.627	20.637	34.874	1.00	10.89		C
ANISOU	1005	CD2	LEU	1273	1779	858	1501	-156	60	116	C
ATOM	1006	C	LEU	1273	19.254	16.973	33.300	1.00	7.53		C
ANISOU	1006	C	LEU	1273	856	835	1171	-73	21	29	C
ATOM	1007	O	LEU	1273	20.444	17.215	33.484	1.00	8.12		O
ANISOU	1007	O	LEU	1273	880	933	1273	-73	3	-56	O
ATOM	1008	N	TRP	1274	18.795	15.693	33.166	1.00	7.61		N
ANISOU	1008	N	TRP	1274	834	853	1205	-9	-20	141	N
ATOM	1009	CA	TRP	1274	19.748	14.576	33.136	1.00	7.75		C
ANISOU	1009	CA	TRP	1274	892	805	1249	-1	91	121	C
ATOM	1010	CB	TRP	1274	18.947	13.271	33.155	1.00	7.89		C
ANISOU	1010	CB	TRP	1274	856	823	1319	-14	-80	144	C
ATOM	1011	CG	TRP	1274	19.754	12.014	33.261	1.00	7.84		C
ANISOU	1011	CG	TRP	1274	930	775	1276	-61	-107	62	C
ATOM	1012	CD2	TRP	1274	20.410	11.289	32.183	1.00	8.33		C
ANISOU	1012	CD2	TRP	1274	1022	812	1332	-54	-96	-17	C
ATOM	1013	CE2	TRP	1274	21.033	10.174	32.795	1.00	8.78		C
ANISOU	1013	CE2	TRP	1274	847	1031	1457	79	-55	4	C

Table 1 (continued)

ATOM	1014	CE3	TRP	1274	20.507	11.480	30.792	1.00	8.97		C
ANISOU	1014	CE3	TRP	1274	873	1170	1366	-71	17	63	C
ATOM	1015	CD1	TRP	1274	20.012	11.329	34.417	1.00	7.88		C
ANISOU	1015	CD1	TRP	1274	794	870	1331	60	-126	146	C
ATOM	1016	NE1	TRP	1274	20.781	10.225	34.141	1.00	8.38		N
ANISOU	1016	NE1	TRP	1274	908	909	1366	86	-183	-22	N
ATOM	1017	CZ2	TRP	1274	21.755	9.256	32.050	1.00	9.41		C
ANISOU	1017	CZ2	TRP	1274	877	1066	1632	107	-65	-164	C
ATOM	1018	CZ3	TRP	1274	21.240	10.538	30.056	1.00	9.83		C
ANISOU	1018	CZ3	TRP	1274	1083	1183	1468	-96	-115	-208	C
ATOM	1019	CH2	TRP	1274	21.859	9.434	30.676	1.00	10.08		C
ANISOU	1019	CH2	TRP	1274	1230	1022	1579	-52	-20	-210	C
ATOM	1020	C	TRP	1274	20.678	14.690	31.930	1.00	7.63		C
ANISOU	1020	C	TRP	1274	783	947	1169	-92	-56	35	C
ATOM	1021	O	TRP	1274	21.883	14.448	32.008	1.00	7.94		O
ANISOU	1021	O	TRP	1274	789	776	1450	25	-17	34	O
ATOM	1022	N	GLU	1275	20.118	15.079	30.765	1.00	7.60		N
ANISOU	1022	N	GLU	1275	951	844	1093	25	17	-42	N
ATOM	1023	CA	GLU	1275	20.958	15.335	29.613	1.00	7.25		C
ANISOU	1023	CA	GLU	1275	745	906	1104	-62	-37	31	C
ATOM	1024	CB	GLU	1275	20.124	15.857	28.453	1.00	7.91		C
ANISOU	1024	CB	GLU	1275	874	962	1171	-28	-115	35	C
ATOM	1025	CG	GLU	1275	19.102	14.852	27.910	1.00	8.53		C
ANISOU	1025	CG	GLU	1275	1005	965	1271	-83	-196	-55	C
ATOM	1026	CD	GLU	1275	18.490	15.454	26.631	1.00	7.60		C
ANISOU	1026	CD	GLU	1275	806	868	1214	-84	-69	-109	C
ATOM	1027	OE1	GLU	1275	17.415	16.099	26.727	1.00	8.22		O1-
ANISOU	1027	OE1	GLU	1275	930	833	1360	-38	-1	-28	O1-
ATOM	1028	OE2	GLU	1275	19.120	15.278	25.564	1.00	8.89		O
ANISOU	1028	OE2	GLU	1275	1031	1115	1232	197	20	34	O
ATOM	1029	C	GLU	1275	22.006	16.386	29.913	1.00	7.37		C
ANISOU	1029	C	GLU	1275	796	820	1184	17	-9	-38	C
ATOM	1030	O	GLU	1275	23.188	16.254	29.564	1.00	8.10		O
ANISOU	1030	O	GLU	1275	723	1057	1297	8	79	107	O
ATOM	1031	N	LEU	1276	21.612	17.473	30.566	1.00	8.03		N
ANISOU	1031	N	LEU	1276	1009	792	1251	24	-33	-19	N
ATOM	1032	CA	LEU	1276	22.585	18.522	30.882	1.00	7.69		C
ANISOU	1032	CA	LEU	1276	923	794	1205	69	-74	-41	C
ATOM	1033	CB	LEU	1276	21.907	19.717	31.573	1.00	8.36		C
ANISOU	1033	CB	LEU	1276	1039	860	1277	130	-96	-146	C
ATOM	1034	CG	LEU	1276	21.092	20.576	30.619	1.00	8.55		C
ANISOU	1034	CG	LEU	1276	1039	742	1468	71	69	78	C
ATOM	1035	CD1	LEU	1276	20.186	21.509	31.374	1.00	9.54		C
ANISOU	1035	CD1	LEU	1276	934	1007	1684	92	71	-223	C
ATOM	1036	CD2	LEU	1276	22.051	21.376	29.727	1.00	12.65		C
ANISOU	1036	CD2	LEU	1276	1597	1480	1728	167	503	392	C
ATOM	1037	C	LEU	1276	23.702	18.001	31.770	1.00	7.87		C
ANISOU	1037	C	LEU	1276	868	886	1238	116	-2	12	C
ATOM	1038	O	LEU	1276	24.879	18.265	31.496	1.00	8.92		O
ANISOU	1038	O	LEU	1276	906	1139	1344	29	-3	36	O
ATOM	1039	N	AMET	1277	23.352	17.251	32.833	0.60	8.18		N

Table 1 (continued)

ANISOU	1039	N	AMET	1277	937	959	1214	21	-145	43	N
ATOM	1040	N	BMET	1277	23.364	17.253	32.826	0.40	7.97		N
ANISOU	1040	N	BMET	1277	922	899	1207	70	-106	24	N
ATOM	1041	CA	AMET	1277	24.340	16.831	33.820	0.60	8.67		C
ANISOU	1041	CA	AMET	1277	971	1016	1308	131	-179	22	C
ATOM	1042	CA	BMET	1277	24.401	16.878	33.786	0.40	8.78		C
ANISOU	1042	CA	BMET	1277	903	1320	1114	200	-34	-21	C
ATOM	1043	CB	AMET	1277	23.677	16.267	35.069	0.60	10.87		C
ANISOU	1043	CB	AMET	1277	1256	1542	1331	329	-18	274	C
ATOM	1044	CB	BMET	1277	23.752	16.593	35.138	0.40	6.87		C
ANISOU	1044	CB	BMET	1277	803	714	1094	-191	-127	-161	C
ATOM	1045	CG	AMET	1277	23.025	17.256	36.035	0.60	11.92		C
ANISOU	1045	CG	AMET	1277	1374	1557	1597	143	109	101	C
ATOM	1046	CG	BMET	1277	22.837	17.708	35.625	0.40	4.28		C
ANISOU	1046	CG	BMET	1277	468	534	626	-226	-324	170	C
ATOM	1047	SD	AMET	1277	24.207	18.553	36.585	0.60	17.60		S
ANISOU	1047	SD	AMET	1277	2384	1895	2409	-246	-4	-173	S
ATOM	1048	SD	BMET	1277	23.523	19.354	35.545	0.40	5.59		S
ANISOU	1048	SD	BMET	1277	678	529	918	-69	-134	200	S
ATOM	1049	CE	AMET	1277	23.669	19.698	35.309	0.60	11.76		C
ANISOU	1049	CE	AMET	1277	1219	1332	1917	-224	477	-533	C
ATOM	1050	CE	BMET	1277	25.057	19.280	36.518	0.40	8.21		C
ANISOU	1050	CE	BMET	1277	623	863	1633	-786	-326	453	C
ATOM	1051	C	AMET	1277	25.314	15.782	33.227	0.60	8.81		C
ANISOU	1051	C	AMET	1277	864	1002	1481	50	-98	48	C
ATOM	1052	C	BMET	1277	25.236	15.673	33.318	0.40	7.75		C
ANISOU	1052	C	BMET	1277	642	1088	1216	31	28	178	C
ATOM	1053	O	AMET	1277	26.424	15.653	33.733	0.60	8.20		O
ANISOU	1053	O	AMET	1277	802	1116	1196	-25	-17	139	O
ATOM	1054	O	BMET	1277	26.183	15.324	34.020	0.40	11.13		O
ANISOU	1054	O	BMET	1277	887	1741	1599	284	-278	120	O
ATOM	1055	N	THR	1278	24.900	15.071	32.182	1.00	8.18		N
ANISOU	1055	N	THR	1278	853	937	1317	38	8	71	N
ATOM	1056	CA	THR	1278	25.754	14.106	31.513	1.00	8.29		C
ANISOU	1056	CA	THR	1278	713	1099	1340	48	29	89	C
ATOM	1057	CB	THR	1278	24.975	12.866	31.074	1.00	8.60		C
ANISOU	1057	CB	THR	1278	976	934	1359	-22	-122	192	C
ATOM	1058	OG1	THR	1278	23.935	13.261	30.113	1.00	8.76		O
ANISOU	1058	OG1	THR	1278	1064	1066	1199	5	-180	162	O
ATOM	1059	CG2	THR	1278	24.296	12.171	32.253	1.00	10.52		C
ANISOU	1059	CG2	THR	1278	1376	1231	1390	33	26	440	C
ATOM	1060	C	THR	1278	26.402	14.708	30.263	1.00	8.50		C
ANISOU	1060	C	THR	1278	916	1088	1227	-9	-1	47	C
ATOM	1061	O	THR	1278	27.090	13.989	29.540	1.00	9.69		O
ANISOU	1061	O	THR	1278	988	1280	1413	87	126	-44	O
ATOM	1062	N	ARG	1279	26.206	15.980	29.966	1.00	8.52		N
ANISOU	1062	N	ARG	1279	737	1088	1414	-77	-72	173	N
ATOM	1063	CA	ARG	1279	26.688	16.652	28.759	1.00	8.82		C
ANISOU	1063	CA	ARG	1279	780	1266	1305	-121	-45	152	C
ATOM	1064	CB	ARG	1279	28.226	16.834	28.758	1.00	9.24		C
ANISOU	1064	CB	ARG	1279	763	1114	1632	-23	35	83	C

Table 1 (continued)

ATOM	1065	CG	ARG	1279	28.597	17.935	29.774	1.00	9.79		C
ANISOU	1065	CG	ARG	1279	786	1608	1326	-87	-18	-87	C
ATOM	1066	CD	ARG	1279	30.079	18.355	29.742	1.00	10.02		C
ANISOU	1066	CD	ARG	1279	772	1494	1542	-61	-62	249	C
ATOM	1067	NE	ARG	1279	30.393	18.852	28.406	1.00	8.98		N
ANISOU	1067	NE	ARG	1279	922	1019	1470	25	142	-97	N
ATOM	1068	CZ	ARG	1279	31.618	19.153	27.986	1.00	9.26		C
ANISOU	1068	CZ	ARG	1279	983	1136	1399	-52	14	-59	C
ATOM	1069	NH1	ARG	1279	32.680	19.032	28.805	1.00	10.05		N1+
ANISOU	1069	NH1	ARG	1279	1004	1147	1668	19	-156	-89	N1+
ATOM	1070	NH2	ARG	1279	31.757	19.589	26.727	1.00	9.97		N
ANISOU	1070	NH2	ARG	1279	1207	1150	1431	-150	83	-6	N
ATOM	1071	C	ARG	1279	26.234	15.916	27.506	1.00	9.12		C
ANISOU	1071	C	ARG	1279	934	1113	1418	-112	83	58	C
ATOM	1072	O	ARG	1279	26.975	15.714	26.525	1.00	9.81		O
ANISOU	1072	O	ARG	1279	943	1422	1363	-131	63	18	O
ATOM	1073	N	GLY	1280	24.936	15.532	27.520	1.00	8.86		N
ANISOU	1073	N	GLY	1280	930	1081	1356	-106	-84	40	N
ATOM	1074	CA	GLY	1280	24.319	15.059	26.277	1.00	9.18		C
ANISOU	1074	CA	GLY	1280	1073	1062	1351	11	-23	-99	C
ATOM	1075	C	GLY	1280	24.429	13.576	26.031	1.00	9.09		C
ANISOU	1075	C	GLY	1280	981	1065	1409	29	-101	-60	C
ATOM	1076	O	GLY	1280	24.359	13.127	24.891	1.00	10.18		O
ANISOU	1076	O	GLY	1280	1074	1331	1463	-45	-31	-205	O
ATOM	1077	N	ALA	1281	24.586	12.781	27.104	1.00	9.80		N
ANISOU	1077	N	ALA	1281	981	1116	1627	82	-140	88	N
ATOM	1078	CA	ALA	1281	24.481	11.344	26.926	1.00	9.73		C
ANISOU	1078	CA	ALA	1281	1043	1060	1596	104	-133	65	C
ATOM	1079	CB	ALA	1281	24.842	10.630	28.213	1.00	10.50		C
ANISOU	1079	CB	ALA	1281	1370	1153	1466	398	-149	-43	C
ATOM	1080	C	ALA	1281	23.068	10.975	26.512	1.00	9.44		C
ANISOU	1080	C	ALA	1281	968	1074	1544	171	-1	-36	C
ATOM	1081	O	ALA	1281	22.089	11.608	26.956	1.00	9.61		O
ANISOU	1081	O	ALA	1281	1061	1187	1403	217	173	170	O
ATOM	1082	N	PRO	1282	22.884	9.973	25.678	1.00	9.87		N
ANISOU	1082	N	PRO	1282	1095	1136	1519	138	-22	-35	N
ATOM	1083	CD	PRO	1282	23.927	9.187	24.997	1.00	11.71		C
ANISOU	1083	CD	PRO	1282	1407	1346	1696	124	184	-328	C
ATOM	1084	CA	PRO	1282	21.525	9.532	25.369	1.00	10.23		C
ANISOU	1084	CA	PRO	1282	1258	1232	1395	-11	-104	-29	C
ATOM	1085	CB	PRO	1282	21.723	8.547	24.209	1.00	12.85		C
ANISOU	1085	CB	PRO	1282	1537	1524	1820	-39	121	-407	C
ATOM	1086	CG	PRO	1282	23.135	8.044	24.391	1.00	13.75		C
ANISOU	1086	CG	PRO	1282	1582	1478	2167	19	56	-502	C
ATOM	1087	C	PRO	1282	20.913	8.822	26.559	1.00	10.02		C
ANISOU	1087	C	PRO	1282	986	1306	1515	67	-221	120	C
ATOM	1088	O	PRO	1282	21.531	7.932	27.134	1.00	10.89		O
ANISOU	1088	O	PRO	1282	1289	1315	1532	168	-142	136	O
ATOM	1089	N	PRO	1283	19.679	9.166	26.932	1.00	9.85		N
ANISOU	1089	N	PRO	1283	1192	1088	1463	79	-83	4	N
ATOM	1090	CD	PRO	1283	18.790	10.166	26.298	1.00	11.10		C

Table 1 (continued)

ANISOU	1090	CD	PRO	1283	960	1434	1824	215	29	184	C
ATOM	1091	CA	PRO	1283	19.102	8.514	28.097	1.00	9.94		C
ANISOU	1091	CA	PRO	1283	1162	991	1623	-25	20	-115	C
ATOM	1092	CB	PRO	1283	17.848	9.384	28.396	1.00	10.86		C
ANISOU	1092	CB	PRO	1283	1321	1019	1787	243	105	94	C
ATOM	1093	CG	PRO	1283	17.477	9.956	27.036	1.00	12.81		C
ANISOU	1093	CG	PRO	1283	1193	1779	1894	165	181	365	C
ATOM	1094	C	PRO	1283	18.716	7.078	27.797	1.00	9.02		C
ANISOU	1094	C	PRO	1283	903	1025	1499	83	-50	-109	C
ATOM	1095	O	PRO	1283	18.275	6.736	26.685	1.00	11.14		O
ANISOU	1095	O	PRO	1283	1608	1111	1513	88	-180	-179	O
ATOM	1096	N	TYR	1284	18.861	6.224	28.820	1.00	9.82		N
ANISOU	1096	N	TYR	1284	1282	921	1529	204	-7	-28	N
ATOM	1097	CA	TYR	1284	18.488	4.795	28.699	1.00	10.89		C
ANISOU	1097	CA	TYR	1284	1184	1061	1893	-187	227	-175	C
ATOM	1098	CB	TYR	1284	16.993	4.630	28.709	1.00	10.86		C
ANISOU	1098	CB	TYR	1284	1189	1141	1797	152	147	96	C
ATOM	1099	CG	TYR	1284	16.100	5.425	29.588	1.00	9.12		C
ANISOU	1099	CG	TYR	1284	1052	873	1542	-6	-68	33	C
ATOM	1100	CD1	TYR	1284	15.832	5.089	30.914	1.00	9.13		C
ANISOU	1100	CD1	TYR	1284	1094	818	1558	-83	-101	-68	C
ATOM	1101	CE1	TYR	1284	14.976	5.872	31.686	1.00	10.08		C
ANISOU	1101	CE1	TYR	1284	1264	999	1567	77	-125	-52	C
ATOM	1102	CD2	TYR	1284	15.467	6.557	29.072	1.00	9.50		C
ANISOU	1102	CD2	TYR	1284	1061	981	1566	21	-3	2	C
ATOM	1103	CE2	TYR	1284	14.618	7.336	29.828	1.00	9.08		C
ANISOU	1103	CE2	TYR	1284	961	956	1531	-78	97	-7	C
ATOM	1104	CZ	TYR	1284	14.377	6.990	31.153	1.00	9.18		C
ANISOU	1104	CZ	TYR	1284	1091	1075	1324	138	-184	-40	C
ATOM	1105	OH	TYR	1284	13.518	7.745	31.917	1.00	9.70		O
ANISOU	1105	OH	TYR	1284	1099	1109	1477	-38	27	-130	O
ATOM	1106	C	TYR	1284	19.051	4.138	27.434	1.00	10.15		C
ANISOU	1106	C	TYR	1284	1240	900	1718	35	160	-20	C
ATOM	1107	O	TYR	1284	18.315	3.573	26.608	1.00	12.75		O
ANISOU	1107	O	TYR	1284	1671	1127	2046	137	-62	-307	O
ATOM	1108	N	PRO	1285	20.373	4.177	27.278	1.00	12.27		N
ANISOU	1108	N	PRO	1285	1300	1273	2088	157	229	-39	N
ATOM	1109	CD	PRO	1285	21.376	4.664	28.228	1.00	12.83		C
ANISOU	1109	CD	PRO	1285	1070	1399	2405	224	103	-35	C
ATOM	1110	CA	PRO	1285	20.969	3.676	26.030	1.00	14.09		C
ANISOU	1110	CA	PRO	1285	1375	1503	2474	157	459	-299	C
ATOM	1111	CB	PRO	1285	22.470	3.981	26.220	1.00	15.60		C
ANISOU	1111	CB	PRO	1285	1455	1820	2651	-128	468	-269	C
ATOM	1112	CG	PRO	1285	22.655	3.937	27.715	1.00	15.06		C
ANISOU	1112	CG	PRO	1285	1323	1715	2686	462	288	-231	C
ATOM	1113	C	PRO	1285	20.786	2.181	25.828	1.00	14.02		C
ANISOU	1113	C	PRO	1285	1454	1539	2333	94	157	-356	C
ATOM	1114	O	PRO	1285	20.875	1.671	24.703	1.00	17.93		O
ANISOU	1114	O	PRO	1285	2295	2012	2504	0	523	-620	O
ATOM	1115	N	ASP	1286	20.525	1.455	26.918	1.00	14.10		N
ANISOU	1115	N	ASP	1286	1546	1380	2431	136	-46	-283	N

Table 1 (continued)

ATOM	1116	CA	ASP	1286	20.315	0.000	26.835	1.00	17.44		C
ANISOU	1116	CA	ASP	1286	1836	1272	3517	213	-259	-202	C
ATOM	1117	CB	ASP	1286	20.965	-0.669	28.044	1.00	24.27		C
ANISOU	1117	CB	ASP	1286	2717	1955	4551	514	-913	435	C
ATOM	1118	CG	ASP	1286	22.479	-0.590	27.904	1.00	28.57		C
ANISOU	1118	CG	ASP	1286	2638	3913	4303	332	-1271	-100	C
ATOM	1119	OD1	ASP	1286	22.982	-0.181	26.823	1.00	37.07		O
ANISOU	1119	OD1	ASP	1286	3849	3660	6576	1228	736	1149	O
ATOM	1120	OD2	ASP	1286	23.144	-0.941	28.900	1.00	47.33		O1-
ANISOU	1120	OD2	ASP	1286	4041	7871	6072	2284	-2396	554	O1-
ATOM	1121	C	ASP	1286	18.844	-0.406	26.749	1.00	17.94		C
ANISOU	1121	C	ASP	1286	1867	1132	3817	64	-86	228	C
ATOM	1122	O	ASP	1286	18.505	-1.600	26.782	1.00	27.24		O
ANISOU	1122	O	ASP	1286	2488	1203	6658	-117	159	-183	O
ATOM	1123	N	VAL	1287	17.940	0.546	26.638	1.00	14.90		N
ANISOU	1123	N	VAL	1287	1697	1322	2641	17	-351	-189	N
ATOM	1124	CA	VAL	1287	16.528	0.284	26.472	1.00	15.30		C
ANISOU	1124	CA	VAL	1287	1783	1575	2453	-38	-355	-157	C
ATOM	1125	CB	VAL	1287	15.722	1.222	27.381	1.00	13.84		C
ANISOU	1125	CB	VAL	1287	1627	1365	2267	-165	-282	-11	C
ATOM	1126	CG1	VAL	1287	14.234	1.030	27.137	1.00	17.31		C
ANISOU	1126	CG1	VAL	1287	1608	1773	3195	-125	-426	34	C
ATOM	1127	CG2	VAL	1287	16.148	0.975	28.841	1.00	17.18		C
ANISOU	1127	CG2	VAL	1287	2438	1808	2281	53	-446	147	C
ATOM	1128	C	VAL	1287	16.119	0.464	25.009	1.00	14.23		C
ANISOU	1128	C	VAL	1287	1773	1246	2389	7	-248	-77	C
ATOM	1129	O	VAL	1287	16.454	1.536	24.446	1.00	17.83		O
ANISOU	1129	O	VAL	1287	2402	1381	2990	-115	-199	234	O
ATOM	1130	N	ASN	1288	15.440	-0.497	24.408	1.00	14.23		N
ANISOU	1130	N	ASN	1288	1832	1235	2340	264	-317	-285	N
ATOM	1131	CA	ASN	1288	14.956	-0.448	23.041	1.00	15.93		C
ANISOU	1131	CA	ASN	1288	2209	1533	2311	329	-352	-228	C
ATOM	1132	CB	ASN	1288	14.823	-1.882	22.491	1.00	18.95		C
ANISOU	1132	CB	ASN	1288	2950	1732	2517	481	-515	-656	C
ATOM	1133	CG	ASN	1288	14.220	-1.892	21.083	1.00	24.51		C
ANISOU	1133	CG	ASN	1288	4244	2704	2366	-713	-568	-357	C
ATOM	1134	OD1	ASN	1288	14.576	-1.077	20.195	1.00	34.15		O
ANISOU	1134	OD1	ASN	1288	7111	3404	2459	-754	287	-67	O
ATOM	1135	ND2	ASN	1288	13.285	-2.819	20.819	1.00	29.42		N
ANISOU	1135	ND2	ASN	1288	3722	3729	3727	-717	-1030	-963	N
ATOM	1136	C	ASN	1288	13.630	0.274	22.978	1.00	14.34		C
ANISOU	1136	C	ASN	1288	2093	1406	1950	217	-191	213	C
ATOM	1137	O	ASN	1288	12.612	-0.327	23.370	1.00	15.29		O
ANISOU	1137	O	ASN	1288	2304	1335	2171	44	-35	-175	O
ATOM	1138	N	THR	1289	13.646	1.523	22.507	1.00	14.85		N
ANISOU	1138	N	THR	1289	2399	1452	1792	206	-81	191	N
ATOM	1139	CA	THR	1289	12.440	2.334	22.237	1.00	14.27		C
ANISOU	1139	CA	THR	1289	2329	1177	1914	45	-280	133	C
ATOM	1140	CB	THR	1289	11.947	2.131	20.793	1.00	17.15		C
ANISOU	1140	CB	THR	1289	2537	1917	2063	-132	-506	-36	C
ATOM	1141	OG1	THR	1289	11.497	0.786	20.551	1.00	18.53		O

Table 1 (continued)

ANISOU	1141	OG1	THR	1289	3124	1705	2212	120	-798	-179	O
ATOM	1142	CG2	THR	1289	13.112	2.394	19.826	1.00	19.29		C
ANISOU	1142	CG2	THR	1289	3187	2077	2066	473	3	165	C
ATOM	1143	C	THR	1289	11.267	2.080	23.210	1.00	13.76		C
ANISOU	1143	C	THR	1289	2146	932	2148	-82	-340	109	C
ATOM	1144	O	THR	1289	11.455	2.451	24.381	1.00	13.13		O
ANISOU	1144	O	THR	1289	1869	1017	2101	71	-250	-99	O
ATOM	1145	N	PHE	1290	10.146	1.495	22.804	1.00	14.90		N
ANISOU	1145	N	PHE	1290	2056	1300	2308	26	-674	170	N
ATOM	1146	CA	PHE	1290	8.945	1.402	23.664	1.00	13.95		C
ANISOU	1146	CA	PHE	1290	1935	1139	2226	-109	-848	107	C
ATOM	1147	CB	PHE	1290	7.676	1.021	22.878	1.00	17.44		C
ANISOU	1147	CB	PHE	1290	2222	1820	2584	-500	-1181	609	C
ATOM	1148	CG	PHE	1290	7.163	2.129	21.962	1.00	16.44		C
ANISOU	1148	CG	PHE	1290	2105	1652	2491	-346	-1115	402	C
ATOM	1149	CD1	PHE	1290	6.317	3.082	22.506	1.00	18.65		C
ANISOU	1149	CD1	PHE	1290	2029	1914	3145	-328	-937	344	C
ATOM	1150	CD2	PHE	1290	7.519	2.203	20.617	1.00	19.19		C
ANISOU	1150	CD2	PHE	1290	2380	2460	2451	-348	-1120	579	C
ATOM	1151	CE1	PHE	1290	5.801	4.125	21.728	1.00	18.42		C
ANISOU	1151	CE1	PHE	1290	2344	1887	2769	2	-558	244	C
ATOM	1152	CE2	PHE	1290	7.011	3.237	19.825	1.00	17.26		C
ANISOU	1152	CE2	PHE	1290	2400	1991	2166	-256	-948	167	C
ATOM	1153	CZ	PHE	1290	6.159	4.178	20.395	1.00	18.62		C
ANISOU	1153	CZ	PHE	1290	2216	2050	2809	-522	-457	142	C
ATOM	1154	C	PHE	1290	9.128	0.415	24.806	1.00	13.58		C
ANISOU	1154	C	PHE	1290	1834	1240	2085	12	-740	22	C
ATOM	1155	O	PHE	1290	8.238	0.349	25.685	1.00	14.33		O
ANISOU	1155	O	PHE	1290	1775	1086	2582	-56	-514	195	O
ATOM	1156	N	ASP	1291	10.257	-0.322	24.864	1.00	12.85		N
ANISOU	1156	N	ASP	1291	2087	818	1977	99	-472	17	N
ATOM	1157	CA	ASP	1291	10.524	-1.062	26.105	1.00	12.06		C
ANISOU	1157	CA	ASP	1291	1764	854	1964	77	-263	112	C
ATOM	1158	CB	ASP	1291	11.803	-1.897	25.962	1.00	12.20		C
ANISOU	1158	CB	ASP	1291	1820	879	1936	123	-193	128	C
ATOM	1159	CG	ASP	1291	11.744	-2.973	24.911	1.00	12.79		C
ANISOU	1159	CG	ASP	1291	1856	1006	1998	84	-138	50	C
ATOM	1160	OD1	ASP	1291	10.728	-3.106	24.228	1.00	15.16		O
ANISOU	1160	OD1	ASP	1291	1897	1210	2652	-231	-217	-255	O
ATOM	1161	OD2	ASP	1291	12.797	-3.669	24.780	1.00	13.94		O1-
ANISOU	1161	OD2	ASP	1291	1902	961	2434	34	17	-42	O1-
ATOM	1162	C	ASP	1291	10.656	-0.156	27.312	1.00	10.93		C
ANISOU	1162	C	ASP	1291	1373	912	1869	22	-133	158	C
ATOM	1163	O	ASP	1291	10.598	-0.630	28.465	1.00	12.35		O
ANISOU	1163	O	ASP	1291	1708	1070	1915	22	-175	206	O
ATOM	1164	N	ILE	1292	10.837	1.146	27.102	1.00	11.08		N
ANISOU	1164	N	ILE	1292	1382	957	1870	-33	-234	44	N
ATOM	1165	CA	ILE	1292	10.905	2.109	28.203	1.00	11.68		C
ANISOU	1165	CA	ILE	1292	1515	1051	1871	-52	69	-68	C
ATOM	1166	CB	ILE	1292	11.158	3.541	27.684	1.00	11.37		C
ANISOU	1166	CB	ILE	1292	1459	1078	1782	-183	-145	-5	C

Table 1 (continued)

ATOM	1167	CG2	ILE	1292	10.001	4.079	26.875	1.00	14.15		C
ANISOU	1167	CG2	ILE	1292	1677	1164	2535	-115	-615	-126	C
ATOM	1168	CG1	ILE	1292	11.488	4.548	28.796	1.00	13.35		C
ANISOU	1168	CG1	ILE	1292	2080	1085	1907	-49	-391	-77	C
ATOM	1169	CD1	ILE	1292	12.724	4.220	29.630	1.00	17.87		C
ANISOU	1169	CD1	ILE	1292	2081	2579	2129	-499	-638	73	C
ATOM	1170	C	ILE	1292	9.629	2.034	29.033	1.00	11.11		C
ANISOU	1170	C	ILE	1292	1484	1207	1530	-115	-192	179	C
ATOM	1171	O	ILE	1292	9.671	2.278	30.246	1.00	12.66		O
ANISOU	1171	O	ILE	1292	1927	1316	1565	-357	-74	20	O
ATOM	1172	N	THR	1293	8.446	1.736	28.473	1.00	11.48		N
ANISOU	1172	N	THR	1293	1499	900	1963	-122	-116	-134	N
ATOM	1173	CA	THR	1293	7.242	1.805	29.278	1.00	12.74		C
ANISOU	1173	CA	THR	1293	1481	1209	2149	-154	-40	-37	C
ATOM	1174	CB	THR	1293	6.019	1.546	28.364	1.00	12.59		C
ANISOU	1174	CB	THR	1293	1505	1187	2093	89	-97	-141	C
ATOM	1175	OG1	THR	1293	6.126	2.416	27.231	1.00	13.51		O
ANISOU	1175	OG1	THR	1293	1771	1186	2177	-26	-233	-107	O
ATOM	1176	CG2	THR	1293	4.707	1.832	29.101	1.00	15.53		C
ANISOU	1176	CG2	THR	1293	1496	1807	2599	-5	42	-271	C
ATOM	1177	C	THR	1293	7.299	0.808	30.394	1.00	12.25		C
ANISOU	1177	C	THR	1293	1652	1158	1844	-148	-93	-232	C
ATOM	1178	O	THR	1293	7.003	1.152	31.554	1.00	13.63		O
ANISOU	1178	O	THR	1293	1806	1340	2035	-423	155	-426	O
ATOM	1179	N	AVAL	1294	7.678	-0.449	30.076	0.50	12.24		N
ANISOU	1179	N	AVAL	1294	1764	1122	1764	-296	189	-130	N
ATOM	1180	N	BVAL	1294	7.680	-0.449	30.101	0.50	12.62		N
ANISOU	1180	N	BVAL	1294	1714	1207	1872	-82	81	-153	N
ATOM	1181	CA	AVAL	1294	7.750	-1.477	31.112	0.50	13.37		C
ANISOU	1181	CA	AVAL	1294	1870	1251	1960	-35	-61	-30	C
ATOM	1182	CA	BVAL	1294	7.637	-1.380	31.248	0.50	12.58		C
ANISOU	1182	CA	BVAL	1294	1914	1005	1862	-118	41	-290	C
ATOM	1183	CB	AVAL	1294	8.106	-2.885	30.603	0.50	16.96		C
ANISOU	1183	CB	AVAL	1294	2971	1129	2344	-292	-108	-172	C
ATOM	1184	CB	BVAL	1294	7.613	-2.819	30.743	0.50	14.22		C
ANISOU	1184	CB	BVAL	1294	2223	1102	2078	29	541	-427	C
ATOM	1185	CG1AVAL		1294	6.972	-3.509	29.788	0.50	19.44		C
ANISOU	1185	CG1AVAL		1294	3434	1959	1996	-893	5	-255	C
ATOM	1186	CG1BVAL		1294	8.995	-3.263	30.287	0.50	14.49		C
ANISOU	1186	CG1BVAL		1294	1831	935	2739	-462	578	-567	C
ATOM	1187	CG2AVAL		1294	9.369	-2.830	29.778	0.50	21.70		C
ANISOU	1187	CG2AVAL		1294	2509	2236	3501	757	3	-716	C
ATOM	1188	CG2BVAL		1294	7.120	-3.769	31.825	0.50	11.88		C
ANISOU	1188	CG2BVAL		1294	1330	965	2219	-149	88	-344	C
ATOM	1189	C	AVAL	1294	8.787	-1.067	32.169	0.50	12.41		C
ANISOU	1189	C	AVAL	1294	1677	1145	1892	-2	152	-112	C
ATOM	1190	C	BVAL	1294	8.793	-1.067	32.195	0.50	12.52		C
ANISOU	1190	C	BVAL	1294	1606	1233	1918	55	132	-35	C

Table 1 (continued)

ATOM	1191	O	AVAL	1294	8.537	-1.255	33.351	0.50	13.31		O
ANISOU	1191	O	AVAL	1294	1949	1231	1878	-251	67	-71	O
ATOM	1192	O	BVAL	1294	8.659	-1.322	33.389	0.50	13.03		O
ANISOU	1192	O	BVAL	1294	1973	1099	1880	-274	7	-94	O
ATOM	1193	N	TYR	1295	9.912	-0.521	31.732	1.00	12.59		N
ANISOU	1193	N	TYR	1295	1548	1105	2130	121	181	-45	N
ATOM	1194	CA	TYR	1295	10.946	-0.077	32.663	1.00	12.93		C
ANISOU	1194	CA	TYR	1295	1597	1055	2259	83	162	47	C
ATOM	1195	CB	TYR	1295	12.074	0.570	31.834	1.00	13.69		C
ANISOU	1195	CB	TYR	1295	1529	1309	2362	65	231	84	C
ATOM	1196	CG	TYR	1295	13.306	1.008	32.560	1.00	16.70		C
ANISOU	1196	CG	TYR	1295	1600	2363	2383	-55	15	374	C
ATOM	1197	CD1	TYR	1295	13.521	2.318	32.986	1.00	18.98		C
ANISOU	1197	CD1	TYR	1295	2027	2631	2553	-866	-278	405	C
ATOM	1198	CE1	TYR	1295	14.688	2.689	33.664	1.00	23.05		C
ANISOU	1198	CE1	TYR	1295	1897	3650	3210	-1215	-327	731	C
ATOM	1199	CD2	TYR	1295	14.286	0.033	32.812	1.00	22.87		C
ANISOU	1199	CD2	TYR	1295	1425	3782	3481	654	366	474	C
ATOM	1200	CE2	TYR	1295	15.450	0.368	33.483	1.00	25.34		C
ANISOU	1200	CE2	TYR	1295	1451	4818	3358	456	298	974	C
ATOM	1201	CZ	TYR	1295	15.616	1.682	33.889	1.00	27.73		C
ANISOU	1201	CZ	TYR	1295	2055	4873	3606	-619	-295	1321	C
ATOM	1202	OH	TYR	1295	16.791	1.946	34.540	1.00	41.40		O
ANISOU	1202	OH	TYR	1295	2025	6425	7278	-424	-1235	534	O
ATOM	1203	C	TYR	1295	10.406	0.909	33.684	1.00	12.05		C
ANISOU	1203	C	TYR	1295	1404	1075	2100	12	26	68	C
ATOM	1204	O	TYR	1295	10.609	0.806	34.901	1.00	12.19		O
ANISOU	1204	O	TYR	1295	1386	1033	2212	-7	-57	54	O
ATOM	1205	N	LEU	1296	9.692	1.921	33.180	1.00	11.10		N
ANISOU	1205	N	LEU	1296	1358	983	1875	-27	-111	-163	N
ATOM	1206	CA	LEU	1296	9.104	2.947	34.075	1.00	11.39		C
ANISOU	1206	CA	LEU	1296	1657	825	1844	-104	37	-31	C
ATOM	1207	CB	LEU	1296	8.602	4.108	33.226	1.00	11.71		C
ANISOU	1207	CB	LEU	1296	1477	862	2111	-88	-250	-25	C
ATOM	1208	CG	LEU	1296	9.695	4.840	32.445	1.00	11.33		C
ANISOU	1208	CG	LEU	1296	1564	1000	1742	-142	-394	93	C
ATOM	1209	CD1	LEU	1296	9.018	5.826	31.512	1.00	13.82		C
ANISOU	1209	CD1	LEU	1296	1853	1261	2138	-23	-580	337	C
ATOM	1210	CD2	LEU	1296	10.697	5.535	33.370	1.00	12.80		C
ANISOU	1210	CD2	LEU	1296	1577	1224	2061	-320	-529	189	C
ATOM	1211	C	LEU	1296	7.997	2.380	34.948	1.00	12.19		C
ANISOU	1211	C	LEU	1296	1413	1177	2041	-120	58	-98	C
ATOM	1212	O	LEU	1296	7.880	2.764	36.131	1.00	12.57		O
ANISOU	1212	O	LEU	1296	1609	1139	2027	-108	119	-38	O
ATOM	1213	N	LEU	1297	7.175	1.468	34.425	1.00	12.98		N
ANISOU	1213	N	LEU	1297	1359	1241	2332	-163	2	-110	N
ATOM	1214	CA	LEU	1297	6.085	0.876	35.190	1.00	13.37		C
ANISOU	1214	CA	LEU	1297	1535	1174	2371	-129	228	-250	C
ATOM	1215	CB	LEU	1297	5.253	-0.064	34.325	1.00	15.81		C
ANISOU	1215	CB	LEU	1297	1672	1580	2754	-408	-129	-224	C
ATOM	1216	CG	LEU	1297	4.137	0.522	33.496	1.00	24.97		C

Table 1 (continued)

ANISOU	1216	CG	LEU	1297	2366	3080	4042	709	-933	-1004	C
ATOM	1217	CD1	LEU	1297	3.535	-0.491	32.499	1.00	29.70		C
ANISOU	1217	CD1	LEU	1297	3214	4972	3100	-1962	-776	-124	C
ATOM	1218	CD2	LEU	1297	3.036	1.088	34.412	1.00	25.27		C
ANISOU	1218	CD2	LEU	1297	1734	2293	5575	-73	496	451	C
ATOM	1219	C	LEU	1297	6.630	0.090	36.353	1.00	13.35		C
ANISOU	1219	C	LEU	1297	1487	1307	2277	-284	204	-238	C
ATOM	1220	O	LEU	1297	6.005	-0.032	37.398	1.00	16.83		O
ANISOU	1220	O	LEU	1297	1743	2265	2388	-268	382	-49	O
ATOM	1221	N	GLN	1298	7.826	-0.475	36.126	1.00	13.14		N
ANISOU	1221	N	GLN	1298	1547	1100	2344	-189	102	-165	N
ATOM	1222	CA	GLN	1298	8.514	-1.213	37.187	1.00	14.79		C
ANISOU	1222	CA	GLN	1298	1888	1320	2412	-195	-89	-154	C
ATOM	1223	CB	GLN	1298	9.698	-2.080	36.639	1.00	14.60		C
ANISOU	1223	CB	GLN	1298	2129	1050	2370	-10	-235	-115	C
ATOM	1224	CG	GLN	1298	9.137	-3.284	35.839	1.00	16.14		C
ANISOU	1224	CG	GLN	1298	2391	1439	2301	-151	-269	-271	C
ATOM	1225	CD	GLN	1298	10.257	-3.994	35.071	1.00	17.61		C
ANISOU	1225	CD	GLN	1298	2519	1269	2902	111	-280	-403	C
ATOM	1226	OE1	GLN	1298	11.399	-3.520	35.017	1.00	20.58		O
ANISOU	1226	OE1	GLN	1298	2488	2013	3318	-32	-79	-836	O
ATOM	1227	NE2	GLN	1298	9.950	-5.114	34.455	1.00	18.17		N
ANISOU	1227	NE2	GLN	1298	3259	1285	2362	-145	-214	-165	N
ATOM	1228	C	GLN	1298	9.076	-0.313	38.262	1.00	14.49		C
ANISOU	1228	C	GLN	1298	1676	1420	2411	-122	-13	-220	C
ATOM	1229	O	GLN	1298	9.613	-0.807	39.270	1.00	16.52		O
ANISOU	1229	O	GLN	1298	2394	1525	2356	-188	-161	-191	O
ATOM	1230	N	GLY	1299	8.992	1.000	38.086	1.00	14.57		N
ANISOU	1230	N	GLY	1299	1834	1359	2343	-320	-40	-286	N
ATOM	1231	CA	GLY	1299	9.503	1.938	39.077	1.00	13.13		C
ANISOU	1231	CA	GLY	1299	1660	1597	1731	-240	-83	-151	C
ATOM	1232	C	GLY	1299	10.994	2.146	38.923	1.00	14.42		C
ANISOU	1232	C	GLY	1299	1687	1478	2314	-329	2	-72	C
ATOM	1233	O	GLY	1299	11.634	2.495	39.943	1.00	19.79		O
ANISOU	1233	O	GLY	1299	1909	2665	2945	-587	-200	-1032	O
ATOM	1234	N	ARG	1300	11.538	1.956	37.722	1.00	12.49		N
ANISOU	1234	N	ARG	1300	1443	985	2319	-54	-46	324	N
ATOM	1235	CA	ARG	1300	12.958	2.245	37.479	1.00	12.31		C
ANISOU	1235	CA	ARG	1300	1442	878	2359	-15	-23	92	C
ATOM	1236	CB	ARG	1300	13.503	1.138	36.580	1.00	12.64		C
ANISOU	1236	CB	ARG	1300	1733	1022	2048	15	-88	54	C
ATOM	1237	CG	ARG	1300	13.324	-0.231	37.232	1.00	15.33		C
ANISOU	1237	CG	ARG	1300	2503	940	2380	198	-38	65	C
ATOM	1238	CD	ARG	1300	13.770	-1.361	36.288	1.00	15.58		C
ANISOU	1238	CD	ARG	1300	2458	1169	2291	598	-241	23	C
ATOM	1239	NE	ARG	1300	13.432	-2.651	36.872	1.00	16.28		N
ANISOU	1239	NE	ARG	1300	2495	1142	2550	428	-430	0	N
ATOM	1240	CZ	ARG	1300	14.156	-3.285	37.808	1.00	16.09		C
ANISOU	1240	CZ	ARG	1300	2226	1481	2408	240	-346	280	C
ATOM	1241	NH1	ARG	1300	13.742	-4.476	38.281	1.00	17.75		N1+
ANISOU	1241	NH1	ARG	1300	3094	1528	2124	-174	-597	180	N1+

Table 1 (continued)

ATOM	1242	NH2	ARG	1300	15.293	-2.742	38.272	1.00	15.38		N
ANISOU	1242	NH2	ARG	1300	2371	1576	1895	161	-119	-188	N
ATOM	1243	C	ARG	1300	13.084	3.641	36.895	1.00	11.27		C
ANISOU	1243	C	ARG	1300	1213	918	2151	-22	-68	34	C
ATOM	1244	O	ARG	1300	12.148	4.125	36.239	1.00	10.63		O
ANISOU	1244	O	ARG	1300	1401	909	1728	42	-68	-67	O
ATOM	1245	N	ARG	1301	14.211	4.284	37.132	1.00	10.94		N
ANISOU	1245	N	ARG	1301	1320	939	1897	-68	-35	189	N
ATOM	1246	CA	ARG	1301	14.462	5.649	36.726	1.00	9.18		C
ANISOU	1246	CA	ARG	1301	1214	732	1540	42	175	21	C
ATOM	1247	CB	ARG	1301	14.179	6.652	37.855	1.00	9.72		C
ANISOU	1247	CB	ARG	1301	993	1255	1444	49	-67	-172	C
ATOM	1248	CG	ARG	1301	12.717	6.628	38.327	1.00	9.44		C
ANISOU	1248	CG	ARG	1301	997	989	1600	63	27	-9	C
ATOM	1249	CD	ARG	1301	11.782	7.195	37.280	1.00	9.52		C
ANISOU	1249	CD	ARG	1301	969	894	1753	48	37	138	C
ATOM	1250	NE	ARG	1301	10.391	7.404	37.708	1.00	9.24		N
ANISOU	1250	NE	ARG	1301	988	852	1672	15	9	241	N
ATOM	1251	CZ	ARG	1301	9.441	6.518	37.577	1.00	9.53		C
ANISOU	1251	CZ	ARG	1301	1063	837	1719	1	28	168	C
ATOM	1252	NHI	ARG	1301	9.649	5.292	37.037	1.00	10.23		N1+
ANISOU	1252	NH1	ARG	1301	1245	952	1691	26	-19	-112	N1+
ATOM	1253	NH2	ARG	1301	8.206	6.819	37.995	1.00	10.44		N
ANISOU	1253	NH2	ARG	1301	1036	1088	1841	69	165	160	N
ATOM	1254	C	ARG	1301	15.914	5.784	36.277	1.00	9.87		C
ANISOU	1254	C	ARG	1301	1103	945	1701	58	59	48	C
ATOM	1255	O	ARG	1301	16.764	4.954	36.627	1.00	11.76		O
ANISOU	1255	O	ARG	1301	1172	1075	2222	157	52	343	O
ATOM	1256	N	LEU	1302	16.186	6.859	35.510	1.00	8.85		N
ANISOU	1256	N	LEU	1302	984	1047	1334	-25	1	-10	N
ATOM	1257	CA	LEU	1302	17.563	7.203	35.210	1.00	8.89		C
ANISOU	1257	CA	LEU	1302	1047	1055	1276	-133	-53	0	C
ATOM	1258	CB	LEU	1302	17.604	8.539	34.471	1.00	9.51		C
ANISOU	1258	CB	LEU	1302	1271	1018	1323	-57	-176	26	C
ATOM	1259	CG	LEU	1302	17.043	8.469	33.039	1.00	8.86		C
ANISOU	1259	CG	LEU	1302	1045	1075	1247	-14	-111	-56	C
ATOM	1260	CD1	LEU	1302	16.732	9.859	32.525	1.00	10.17		C
ANISOU	1260	CD1	LEU	1302	1507	1066	1290	-129	-225	38	C
ATOM	1261	CD2	LEU	1302	18.014	7.747	32.101	1.00	10.32		C
ANISOU	1261	CD2	LEU	1302	1048	1389	1485	-147	107	-223	C
ATOM	1262	C	LEU	1302	18.413	7.312	36.483	1.00	8.91		C
ANISOU	1262	C	LEU	1302	1036	977	1372	-40	-92	15	C
ATOM	1263	O	LEU	1302	17.951	7.839	37.487	1.00	9.40		O
ANISOU	1263	O	LEU	1302	1170	1049	1354	-76	-94	-93	O
ATOM	1264	N	LEU	1303	19.651	6.822	36.400	1.00	9.19		N
ANISOU	1264	N	LEU	1303	1092	989	1411	14	-177	22	N
ATOM	1265	CA	LEU	1303	20.583	6.900	37.532	1.00	9.47		C
ANISOU	1265	CA	LEU	1303	1027	1098	1472	57	-150	-77	C
ATOM	1266	CB	LEU	1303	21.753	5.919	37.324	1.00	11.46		C
ANISOU	1266	CB	LEU	1303	1169	1250	1935	256	-215	-145	C
ATOM	1267	CG	LEU	1303	21.346	4.444	37.188	1.00	14.04		C

Table 1 (continued)

ANISOU	1267	CG	LEU	1303	1942	1180	2213	310	40	-75	C
ATOM	1268	CD1	LEU	1303	22.611	3.594	37.006	1.00	19.13		C
ANISOU	1268	CD1	LEU	1303	2562	1580	3127	980	-95	112	C
ATOM	1269	CD2	LEU	1303	20.548	4.001	38.373	1.00	20.51		C
ANISOU	1269	CD2	LEU	1303	3400	1600	2791	27	721	352	C
ATOM	1270	C	LEU	1303	21.131	8.306	37.698	1.00	8.89		C
ANISOU	1270	C	LEU	1303	1028	1057	1293	-28	-114	79	C
ATOM	1271	O	LEU	1303	21.135	9.116	36.725	1.00	10.51		O
ANISOU	1271	O	LEU	1303	1467	1237	1288	-52	-280	134	O
ATOM	1272	N	GLN	1304	21.615	8.631	38.865	1.00	8.82		N
ANISOU	1272	N	GLN	1304	1046	996	1310	-35	-217	218	N
ATOM	1273	CA	GLN	1304	22.186	9.937	39.120	1.00	9.13		C
ANISOU	1273	CA	GLN	1304	1059	1157	1253	-223	-2	62	C
ATOM	1274	CB	GLN	1304	22.413	10.071	40.635	1.00	9.74		C
ANISOU	1274	CB	GLN	1304	1245	1113	1344	-25	-138	54	C
ATOM	1275	CG	GLN	1304	22.960	11.467	41.000	1.00	9.72		C
ANISOU	1275	CG	GLN	1304	1160	1162	1373	-96	-289	129	C
ATOM	1276	CD	GLN	1304	22.981	11.664	42.514	1.00	8.88		C
ANISOU	1276	CD	GLN	1304	1080	915	1381	62	-121	151	C
ATOM	1277	OE1	GLN	1304	22.538	10.822	43.310	1.00	9.87		O
ANISOU	1277	OE1	GLN	1304	1267	1021	1463	-123	-72	240	O
ATOM	1278	NE2	GLN	1304	23.508	12.802	42.961	1.00	9.86		N
ANISOU	1278	NE2	GLN	1304	1131	941	1676	-17	-194	22	N
ATOM	1279	C	GLN	1304	23.490	10.134	38.385	1.00	9.41		C
ANISOU	1279	C	GLN	1304	932	1147	1497	68	1	259	C
ATOM	1280	O	GLN	1304	24.461	9.396	38.605	1.00	11.06		O
ANISOU	1280	O	GLN	1304	1282	1192	1726	172	8	190	O
ATOM	1281	N	PRO	1305	23.633	11.119	37.492	1.00	8.95		N
ANISOU	1281	N	PRO	1305	1043	1129	1227	-48	-37	124	N
ATOM	1282	CD	PRO	1305	22.577	12.016	36.996	1.00	10.56		C
ANISOU	1282	CD	PRO	1305	1103	1589	1320	-103	-146	626	C
ATOM	1283	CA	PRO	1305	24.922	11.382	36.857	1.00	10.76		C
ANISOU	1283	CA	PRO	1305	1104	1553	1430	-216	-10	328	C
ATOM	1284	CB	PRO	1305	24.621	12.600	35.938	1.00	11.11		C
ANISOU	1284	CB	PRO	1305	1075	1601	1547	-105	-15	416	C
ATOM	1285	CG	PRO	1305	23.136	12.444	35.635	1.00	10.89		C
ANISOU	1285	CG	PRO	1305	1163	1611	1363	-328	-16	436	C
ATOM	1286	C	PRO	1305	26.012	11.719	37.868	1.00	10.69		C
ANISOU	1286	C	PRO	1305	1186	1423	1452	-126	-66	282	C
ATOM	1287	O	PRO	1305	25.751	12.325	38.890	1.00	10.80		O
ANISOU	1287	O	PRO	1305	1079	1439	1588	-109	-118	217	O
ATOM	1288	N	GLU	1306	27.241	11.302	37.532	1.00	11.59		N
ANISOU	1288	N	GLU	1306	1186	1524	1694	75	-94	361	N
ATOM	1289	CA	GLU	1306	28.415	11.560	38.338	1.00	13.33		C
ANISOU	1289	CA	GLU	1306	1388	1634	2044	266	-313	206	C
ATOM	1290	CB	GLU	1306	29.689	11.208	37.520	1.00	18.09		C
ANISOU	1290	CB	GLU	1306	1237	2384	3251	749	-253	-189	C
ATOM	1291	CG	GLU	1306	30.945	11.540	38.304	1.00	25.24		C
ANISOU	1291	CG	GLU	1306	1565	4833	3192	-120	-154	-240	C
ATOM	1292	CD	GLU	1306	32.189	11.064	37.585	1.00	29.39		C
ANISOU	1292	CD	GLU	1306	1231	5919	4015	220	-376	-574	C

Table 1 (continued)

ATOM	1293	OE1	GLU	1306	32.125	10.803	36.355	1.00	31.27		O1-
ANISOU	1293	OE1	GLU	1306	1932	5860	4090	883	-94	-983	O1-
ATOM	1294	OE2	GLU	1306	33.236	10.966	38.267	1.00	38.16		O
ANISOU	1294	OE2	GLU	1306	2380	6901	5219	1465	-1343	-355	O
ATOM	1295	C	GLU	1306	28.502	12.993	38.805	1.00	12.43		C
ANISOU	1295	C	GLU	1306	1223	1677	1823	-1	-87	248	C
ATOM	1296	O	GLU	1306	28.813	13.250	39.975	1.00	15.21		O
ANISOU	1296	O	GLU	1306	1833	2028	1919	-271	-470	341	O
ATOM	1297	N	TYR	1307	28.252	13.955	37.918	1.00	12.32		N
ANISOU	1297	N	TYR	1307	1159	1615	1908	17	-94	340	N
ATOM	1298	CA	TYR	1307	28.417	15.375	38.308	1.00	13.42		C
ANISOU	1298	CA	TYR	1307	1344	1605	2149	-156	66	398	C
ATOM	1299	CB	TYR	1307	29.007	16.159	37.145	1.00	13.35		C
ANISOU	1299	CB	TYR	1307	1403	1724	1945	-183	132	239	C
ATOM	1300	CG	TYR	1307	30.476	15.944	36.930	1.00	15.04		C
ANISOU	1300	CG	TYR	1307	1419	1756	2539	-319	133	149	C
ATOM	1301	CD1	TYR	1307	30.941	14.947	36.108	1.00	15.62		C
ANISOU	1301	CD1	TYR	1307	1359	2303	2274	227	-254	3	C
ATOM	1302	CE1	TYR	1307	32.292	14.789	35.937	1.00	18.86		C
ANISOU	1302	CEI	TYR	1307	1432	2835	2901	156	-151	-36	C
ATOM	1303	CD2	TYR	1307	31.389	16.788	37.577	1.00	15.74		C
ANISOU	1303	CD2	TYR	1307	1409	1850	2721	-252	-19	214	C
ATOM	1304	CE2	TYR	1307	32.762	16.620	37.396	1.00	17.81		C
ANISOU	1304	CE2	TYR	1307	1384	2404	2980	-41	-281	306	C
ATOM	1305	CZ	TYR	1307	33.206	15.606	36.566	1.00	18.52		C
ANISOU	1305	CZ	TYR	1307	1213	2209	3614	168	-205	310	C
ATOM	1306	OH	TYR	1307	34.574	15.479	36.418	1.00	25.92		O
ANISOU	1306	OH	TYR	1307	1175	3449	5224	296	39	142	O
ATOM	1307	C	TYR	1307	27.105	16.016	38.741	1.00	13.14		C
ANISOU	1307	C	TYR	1307	1474	1486	2031	-163	190	318	C
ATOM	1308	O	TYR	1307	27.031	17.255	38.955	1.00	15.30		O
ANISOU	1308	O	TYR	1307	1592	1590	2632	-330	273	-25	O
ATOM	1309	N	CYS	1308	26.040	15.218	38.876	1.00	11.46		N
ANISOU	1309	N	CYS	1308	1222	1446	1686	-110	-96	396	N
ATOM	1310	CA	CYS	1308	24.771	15.785	39.316	1.00	11.80		C
ANISOU	1310	CA	CYS	1308	1281	1617	1586	-197	-162	173	C
ATOM	1311	CB	CYS	1308	23.612	14.867	38.858	1.00	11.30		C
ANISOU	1311	CB	CYS	1308	1251	1202	1840	-102	-115	-52	C
ATOM	1312	SG	CYS	1308	21.987	15.498	39.385	1.00	11.19		S
ANISOU	1312	SG	CYS	1308	1269	1366	1616	9	-170	177	S
ATOM	1313	C	CYS	1308	24.736	15.980	40.813	1.00	10.16		C
ANISOU	1313	C	CYS	1308	1156	1110	1593	-102	-247	227	C
ATOM	1314	O	CYS	1308	24.838	14.939	41.502	1.00	11.07		O
ANISOU	1314	O	CYS	1308	1268	1125	1812	-115	-215	290	O
ATOM	1315	N	PRO	1309	24.594	17.153	41.373	1.00	10.30		N
ANISOU	1315	N	PRO	1309	1090	1097	1728	-43	-103	236	N
ATOM	1316	CD	PRO	1309	24.472	18.483	40.727	1.00	12.79		C
ANISOU	1316	CD	PRO	1309	1717	1095	2049	124	-295	247	C
ATOM	1317	CA	PRO	1309	24.520	17.230	42.852	1.00	11.57		C
ANISOU	1317	CA	PRO	1309	1300	1341	1755	-165	74	21	C
ATOM	1318	CB	PRO	1309	24.522	18.734	43.165	1.00	14.62		C

Table 1 (continued)

ANISOU	1318	CB	PRO	1309	2182	1323	2050	-505	271	-29	C
ATOM	1319	CG	PRO	1309	24.151	19.357	41.899	1.00	17.02		C
ANISOU	1319	CG	PRO	1309	2591	1281	2594	419	-887	-331	C
ATOM	1320	C	PRO	1309	23.238	16.578	43.368	1.00	10.22		C
ANISOU	1320	C	PRO	1309	1187	1169	1528	-118	-218	120	C
ATOM	1321	O	PRO	1309	22.194	16.536	42.688	1.00	10.38		O
ANISOU	1321	O	PRO	1309	1239	1109	1596	-21	-237	52	O
ATOM	1322	N	ASP	1310	23.259	16.039	44.591	1.00	10.38		N
ANISOU	1322	N	ASP	1310	1297	1177	1469	-37	-156	23	N
ATOM	1323	CA	ASP	1310	22.125	15.312	45.114	1.00	10.23		C
ANISOU	1323	CA	ASP	1310	1361	1259	1266	-87	-200	115	C
ATOM	1324	CB	ASP	1310	22.414	14.859	46.563	1.00	12.93		C
ANISOU	1324	CB	ASP	1310	2098	1405	1410	80	-361	338	C
ATOM	1325	CG	ASP	1310	23.570	13.919	46.709	1.00	13.66		C
ANISOU	1325	CG	ASP	1310	2192	1415	1584	108	-452	336	C
ATOM	1326	OD1	ASP	1310	24.072	13.349	45.709	1.00	13.07		O
ANISOU	1326	OD1	ASP	1310	1758	1415	1793	-134	-308	252	O
ATOM	1327	OD2	ASP	1310	24.003	13.733	47.901	1.00	17.38		O1-
ANISOU	1327	OD2	ASP	1310	2967	1849	1788	40	-938	410	O1-
ATOM	1328	C	ASP	1310	20.835	16.134	45.081	1.00	9.76		C
ANISOU	1328	C	ASP	1310	1289	1159	1258	-177	-302	15	C
ATOM	1329	O	ASP	1310	19.821	15.556	44.686	1.00	9.91		O
ANISOU	1329	O	ASP	1310	1289	1006	1469	-141	-291	28	O
ATOM	1330	N	PRO	1311	20.790	17.421	45.486	1.00	10.30		N
ANISOU	1330	N	PRO	1311	1361	1072	1479	-214	-317	99	N
ATOM	1331	CD	PRO	1311	21.873	18.217	46.106	1.00	11.37		C
ANISOU	1331	CD	PRO	1311	1669	1107	1546	-98	-518	-103	C
ATOM	1332	CA	PRO	1311	19.514	18.134	45.406	1.00	10.38		C
ANISOU	1332	CA	PRO	1311	1501	1136	1307	-66	-172	-58	C
ATOM	1333	CB	PRO	1311	19.838	19.527	45.957	1.00	11.67		C
ANISOU	1333	CB	PRO	1311	1637	1150	1646	-130	-309	-63	C
ATOM	1334	CG	PRO	1311	21.053	19.277	46.804	1.00	15.64		C
ANISOU	1334	CG	PRO	1311	1744	1851	2348	205	-659	-751	C
ATOM	1335	C	PRO	1311	18.982	18.223	43.976	1.00	9.59		C
ANISOU	1335	C	PRO	1311	1264	1067	1312	-192	-125	126	C
ATOM	1336	O	PRO	1311	17.741	18.267	43.809	1.00	9.87		O
ANISOU	1336	O	PRO	1311	1316	1015	1419	-88	-116	199	O
ATOM	1337	N	LEU	1312	19.826	18.269	42.976	1.00	9.24		N
ANISOU	1337	N	LEU	1312	1278	897	1337	-224	-119	90	N
ATOM	1338	CA	LEU	1312	19.285	18.322	41.598	1.00	9.33		C
ANISOU	1338	CA	LEU	1312	1345	915	1287	-224	-23	89	C
ATOM	1339	CB	LEU	1312	20.354	18.862	40.652	1.00	9.98		C
ANISOU	1339	CB	LEU	1312	1145	1234	1413	47	31	193	C
ATOM	1340	CG	LEU	1312	19.822	19.190	39.238	1.00	9.67		C
ANISOU	1340	CG	LEU	1312	1220	1265	1188	246	114	9	C
ATOM	1341	CD1	LEU	1312	18.846	20.363	39.265	1.00	11.14		C
ANISOU	1341	CD1	LEU	1312	1136	1424	1674	253	-97	137	C
ATOM	1342	CD2	LEU	1312	20.981	19.488	38.314	1.00	11.09		C
ANISOU	1342	CD2	LEU	1312	1288	1353	1572	6	227	115	C
ATOM	1343	C	LEU	1312	18.801	16.950	41.168	1.00	8.84		C
ANISOU	1343	C	LEU	1312	1144	959	1256	22	-107	-8	C

Table 1 (continued)

ATOM	1344	O	LEU	1312	17.830	16.871	40.404	1.00	8.89		O
ANISOU	1344	O	LEU	1312	1084	982	1310	-92	-144	95	O
ATOM	1345	N	TYR	1313	19.443	15.846	41.642	1.00	8.98		N
ANISOU	1345	N	TYR	1313	1153	837	1422	-120	-191	84	N
ATOM	1346	CA	TYR	1313	18.859	14.550	41.343	1.00	8.53		C
ANISOU	1346	CA	TYR	1313	981	862	1398	-5	-90	55	C
ATOM	1347	CB	TYR	1313	19.790	13.433	41.865	1.00	9.20		C
ANISOU	1347	CB	TYR	1313	1040	922	1533	66	-188	53	C
ATOM	1348	CG	TYR	1313	19.374	12.050	41.369	1.00	8.64		C
ANISOU	1348	CG	TYR	1313	999	926	1358	128	-116	87	C
ATOM	1349	CD1	TYR	1313	19.154	11.775	40.030	1.00	8.50		C
ANISOU	1349	CD1	TYR	1313	926	1001	1301	101	-133	82	C
ATOM	1350	CE1	TYR	1313	18.780	10.515	39.592	1.00	8.61		C
ANISOU	1350	CE1	TYR	1313	991	978	1303	95	-154	134	C
ATOM	1351	CD2	TYR	1313	19.213	11.012	42.289	1.00	8.33		C
ANISOU	1351	CD2	TYR	1313	842	968	1356	17	-151	135	C
ATOM	1352	CE2	TYR	1313	18.843	9.726	41.872	1.00	8.36		C
ANISOU	1352	CE2	TYR	1313	977	965	1235	119	-117	93	C
ATOM	1353	CZ	TYR	1313	18.623	9.492	40.512	1.00	8.17		C
ANISOU	1353	CZ	TYR	1313	852	977	1274	90	-95	40	C
ATOM	1354	OH	TYR	1313	18.263	8.221	40.121	1.00	8.89		O
ANISOU	1354	OH	TYR	1313	1037	996	1343	-40	-72	78	O
ATOM	1355	C	TYR	1313	17.484	14.439	41.980	1.00	8.32		C
ANISOU	1355	C	TYR	1313	970	852	1340	-38	-168	59	C
ATOM	1356	O	TYR	1313	16.546	13.905	41.387	1.00	8.80		O
ANISOU	1356	O	TYR	1313	1027	867	1449	-112	-212	170	O
ATOM	1357	N	GLU	1314	17.311	14.957	43.211	1.00	8.79		N
ANISOU	1357	N	GLU	1314	1128	897	1315	-33	-26	92	N
ATOM	1358	CA	GLU	1314	15.978	14.928	43.840	1.00	9.11		C
ANISOU	1358	CA	GLU	1314	1131	1083	1247	15	-100	102	C
ATOM	1359	CB	GLU	1314	16.068	15.522	45.241	1.00	10.28		C
ANISOU	1359	CB	GLU	1314	1474	1111	1319	-99	-97	-58	C
ATOM	1360	CG	GLU	1314	16.887	14.661	46.184	1.00	13.98		C
ANISOU	1360	CG	GLU	1314	2223	1589	1500	-428	-534	490	C
ATOM	1361	CD	GLU	1314	17.282	15.420	47.430	1.00	17.01		C
ANISOU	1361	CD	GLU	1314	2515	2250	1698	-210	-651	108	C
ATOM	1362	OE1	GLU	1314	17.037	16.628	47.582	1.00	19.53		O1-
ANISOU	1362	OE1	GLU	1314	3322	2169	1930	-452	-133	-7	O1-
ATOM	1363	OE2	GLU	1314	17.877	14.756	48.312	1.00	26.91		O
ANISOU	1363	OE2	GLU	1314	5033	2792	2398	-41	-2136	64	O
ATOM	1364	C	GLU	1314	14.968	15.666	42.979	1.00	8.90		C
ANISOU	1364	C	GLU	1314	1133	803	1446	23	-189	-28	C
ATOM	1365	O	GLU	1314	13.830	15.226	42.833	1.00	9.29		O
ANISOU	1365	O	GLU	1314	1048	1026	1455	-7	-9	-146	O
ATOM	1366	N	VAL	1315	15.397	16.803	42.388	1.00	8.90		N
ANISOU	1366	N	VAL	1315	1210	781	1389	63	-202	-37	N
ATOM	1367	CA	VAL	1315	14.496	17.556	41.481	1.00	9.42		C
ANISOU	1367	CA	VAL	1315	1509	745	1327	29	-258	-28	C
ATOM	1368	CB	VAL	1315	15.153	18.885	41.074	1.00	9.87		C
ANISOU	1368	CB	VAL	1315	1542	910	1298	-136	-234	68	C
ATOM	1369	CG1	VAL	1315	14.457	19.537	39.872	1.00	11.28		C

Table 1 (continued)

ANISOU	1369	CG1	VAL	1315	1424	1025	1837	16	-470	294	C
ATOM	1370	CG2	VAL	1315	15.133	19.854	42.263	1.00	12.36		C
ANISOU	1370	CG2	VAL	1315	1903	940	1851	-88	-252	-327	C
ATOM	1371	C	VAL	1315	14.114	16.715	40.267	1.00	8.35		C
ANISOU	1371	C	VAL	1315	1066	829	1278	87	-133	18	C
ATOM	1372	O	VAL	1315	12.937	16.636	39.878	1.00	8.81		O
ANISOU	1372	O	VAL	1315	1147	856	1343	41	-257	60	O
ATOM	1373	N	MET	1316	15.089	16.058	39.643	1.00	8.31		N
ANISOU	1373	N	MET	1316	1178	737	1240	55	-98	83	N
ATOM	1374	CA	MET	1316	14.806	15.179	38.519	1.00	8.12		C
ANISOU	1374	CA	MET	1316	1115	780	1191	30	-46	37	C
ATOM	1375	CB	MET	1316	16.081	14.451	38.033	1.00	9.57		C
ANISOU	1375	CB	MET	1316	1182	1155	1298	48	191	39	C
ATOM	1376	CG	MET	1316	17.096	15.347	37.375	1.00	9.36		C
ANISOU	1376	CG	MET	1316	1139	1085	1332	25	-87	160	C
ATOM	1377	SD	MET	1316	18.574	14.283	37.043	1.00	10.59		S
ANISOU	1377	SD	MET	1316	1169	1286	1570	183	62	137	S
ATOM	1378	CE	MET	1316	19.767	15.577	36.652	1.00	10.80		C
ANISOU	1378	CE	MET	1316	1245	1339	1519	-2	-62	357	C
ATOM	1379	C	MET	1316	13.769	14.138	38.905	1.00	7.73		C
ANISOU	1379	C	MET	1316	876	820	1241	128	-96	116	C
ATOM	1380	O	MET	1316	12.778	13.897	38.204	1.00	8.51		O
ANISOU	1380	O	MET	1316	1051	979	1205	36	-125	1	O
ATOM	1381	N	LEU	1317	14.019	13.496	40.062	1.00	7.64		N
ANISOU	1381	N	LEU	1317	1057	700	1147	56	3	72	N
ATOM	1382	CA	LEU	1317	13.110	12.414	40.479	1.00	8.30		C
ANISOU	1382	CA	LEU	1317	975	890	1289	5	-91	174	C
ATOM	1383	CB	LEU	1317	13.648	11.747	41.741	1.00	8.74		C
ANISOU	1383	CB	LEU	1317	956	973	1391	86	-69	344	C
ATOM	1384	CG	LEU	1317	14.973	11.005	41.584	1.00	8.36		C
ANISOU	1384	CG	LEU	1317	992	915	1268	92	-119	49	C
ATOM	1385	CD1	LEU	1317	15.481	10.605	42.984	1.00	9.08		C
ANISOU	1385	CD1	LEU	1317	1164	1025	1262	136	-220	73	C
ATOM	1386	CD2	LEU	1317	14.845	9.800	40.669	1.00	9.69		C
ANISOU	1386	CD2	LEU	1317	1397	1014	1269	52	-219	29	C
ATOM	1387	C	LEU	1317	11.689	12.920	40.721	1.00	8.15		C
ANISOU	1387	C	LEU	1317	950	856	1292	-7	-175	174	C
ATOM	1388	O	LEU	1317	10.719	12.215	40.427	1.00	8.88		O
ANISOU	1388	O	LEU	1317	988	929	1458	-50	-109	157	O
ATOM	1389	N	LYS	1318	11.564	14.145	41.256	1.00	8.84		N
ANISOU	1389	N	LYS	1318	986	857	1516	22	-2	115	N
ATOM	1390	CA	LYS	1318	10.237	14.724	41.450	1.00	9.39		C
ANISOU	1390	CA	LYS	1318	1096	1067	1405	145	-110	90	C
ATOM	1391	CB	LYS	1318	10.349	16.068	42.136	1.00	11.75		C
ANISOU	1391	CB	LYS	1318	1266	1531	1669	245	-26	-489	C
ATOM	1392	CG	LYS	1318	10.795	16.124	43.575	1.00	17.79		C
ANISOU	1392	CG	LYS	1318	2754	2150	1858	638	-710	-484	C
ATOM	1393	CD	LYS	1318	11.118	17.543	44.042	1.00	25.70		C
ANISOU	1393	CD	LYS	1318	3947	2771	3047	292	-1417	-1306	C
ATOM	1394	CE	LYS	1318	11.580	17.623	45.479	1.00	28.84		C
ANISOU	1394	CE	LYS	1318	4394	4108	2455	-814	-529	-1296	C

Table 1 (continued)

ATOM	1395	NZ	LYS	1318	10.462	17.760	46.451	1.00	33.92		N1+
ANISOU	1395	NZ	LYS	1318	4807	4444	3638	-410	437	733	N1+
ATOM	1396	C	LYS	1318	9.517	14.911	40.115	1.00	8.18		C
ANISOU	1396	C	LYS	1318	932	837	1340	20	-1	116	C
ATOM	1397	O	LYS	1318	8.280	14.728	40.046	1.00	8.98		O
ANISOU	1397	O	LYS	1318	916	1053	1443	31	3	140	O
ATOM	1398	N	CYS	1319	10.247	15.266	39.075	1.00	8.47		N
ANISOU	1398	N	CYS	1319	1071	888	1258	64	-19	66	N
ATOM	1399	CA	CYS	1319	9.677	15.412	37.751	1.00	8.55		C
ANISOU	1399	CA	CYS	1319	1125	883	1240	-45	-34	100	C
ATOM	1400	CB	CYS	1319	10.704	15.975	36.728	1.00	7.71		C
ANISOU	1400	CB	CYS	1319	929	690	1312	-1	-39	105	C
ATOM	1401	SG	CYS	1319	11.231	17.678	37.125	1.00	9.29		S
ANISOU	1401	SG	CYS	1319	1184	878	1467	-93	-132	88	S
ATOM	1402	C	CYS	1319	9.131	14.102	37.162	1.00	8.19		C
ANISOU	1402	C	CYS	1319	855	866	1392	10	-44	101	C
ATOM	1403	O	CYS	1319	8.314	14.142	36.246	1.00	8.74		O
ANISOU	1403	O	CYS	1319	860	955	1505	-31	-92	50	O
ATOM	1404	N	TRP	1320	9.610	12.966	37.699	1.00	8.39		N
ANISOU	1404	N	TRP	1320	928	824	1437	50	-33	96	N
ATOM	1405	CA	TRP	1320	9.215	11.659	37.164	1.00	8.96		C
ANISOU	1405	CA	TRP	1320	779	899	1726	-63	-4	32	C
ATOM	1406	CB	TRP	1320	10.442	10.786	36.861	1.00	9.04		C
ANISOU	1406	CB	TRP	1320	1064	885	1485	101	64	135	C
ATOM	1407	CG	TRP	1320	11.459	11.467	35.966	1.00	7.91		C
ANISOU	1407	CG	TRP	1320	973	823	1208	107	-79	-13	C
ATOM	1408	CD2	TRP	1320	12.888	11.363	36.082	1.00	7.55		C
ANISOU	1408	CD2	TRP	1320	990	687	1191	-42	-134	-100	C
ATOM	1409	CE2	TRP	1320	13.454	12.152	35.052	1.00	7.72		C
ANISOU	1409	CE2	TRP	1320	1053	704	1176	99	-49	-25	C
ATOM	1410	CE3	TRP	1320	13.709	10.685	36.959	1.00	7.69		C
ANISOU	1410	CE3	TRP	1320	1016	568	1337	46	-141	-73	C
ATOM	1411	CD1	TRP	1320	11.216	12.296	34.890	1.00	7.94		C
ANISOU	1411	CD1	TRP	1320	1124	689	1203	3	-119	-59	C
ATOM	1412	NE1	TRP	1320	12.425	12.708	34.339	1.00	8.37		N
ANISOU	1412	NE1	TRP	1320	972	865	1344	-47	-219	8	N
ATOM	1413	CZ2	TRP	1320	14.839	12.257	34.903	1.00	8.35		C
ANISOU	1413	CZ2	TRP	1320	1043	868	1261	116	-80	1	C
ATOM	1414	CZ3	TRP	1320	15.082	10.786	36.816	1.00	8.23		C
ANISOU	1414	CZ3	TRP	1320	1003	777	1348	-29	-222	-13	C
ATOM	1415	CH2	TRP	1320	15.626	11.574	35.786	1.00	8.38		C
ANISOU	1415	CH2	TRP	1320	1036	637	1512	-75	-247	65	C
ATOM	1416	C	TRP	1320	8.252	10.923	38.100	1.00	8.45		C
ANISOU	1416	C	TRP	1320	996	848	1366	29	-131	116	C
ATOM	1417	O	TRP	1320	8.082	9.721	38.024	1.00	9.72		O
ANISOU	1417	O	TRP	1320	1044	862	1788	3	-69	131	O
ATOM	1418	N	HIS	1321	7.583	11.669	38.980	1.00	8.92		N
ANISOU	1418	N	HIS	1321	1016	1103	1272	-95	-44	49	N
ATOM	1419	CA	HIS	1321	6.612	11.050	39.834	1.00	9.13		C
ANISOU	1419	CA	HIS	1321	995	1057	1418	-101	-71	144	C
ATOM	1420	CB	HIS	1321	5.943	12.109	40.706	1.00	9.45		C

Table 1 (continued)

ANISOU	1420	CB	HIS	1321	906	1345	1341	-31	2	193	C
ATOM	1421	CG	HIS	1321	5.210	11.590	41.890	1.00	10.89		C
ANISOU	1421	CG	HIS	1321	985	1715	1439	-53	-20	254	C
ATOM	1422	CD2	HIS	1321	4.073	10.848	41.874	1.00	11.53		C
ANISOU	1422	CD2	HIS	1321	877	1862	1643	-115	72	651	C
ATOM	1423	ND1	HIS	1321	5.550	11.807	43.185	1.00	15.36		N
ANISOU	1423	ND1	HIS	1321	2062	2349	1426	-476	76	327	N
ATOM	1424	CE1	HIS	1321	4.629	11.180	43.938	1.00	14.96		C
ANISOU	1424	CE1	HIS	1321	1152	2956	1576	-61	50	634	C
ATOM	1425	NE2	HIS	1321	3.746	10.604	43.152	1.00	18.70		N
ANISOU	1425	NE2	HIS	1321	1943	3439	1723	-748	57	688	N
ATOM	1426	C	HIS	1321	5.544	10.357	38.990	1.00	9.33		C
ANISOU	1426	C	HIS	1321	1131	955	1460	-122	-192	345	C
ATOM	1427	O	HIS	1321	5.104	10.975	38.022	1.00	9.43		O
ANISOU	1427	O	HIS	1321	1204	1027	1350	-33	-172	289	O
ATOM	1428	N	PRO	1322	5.110	9.140	39.306	1.00	10.76		N
ANISOU	1428	N	PRO	1322	1128	1010	1949	-160	-296	509	N
ATOM	1429	CD	PRO	1322	5.546	8.290	40.411	1.00	11.80		C
ANISOU	1429	CD	PRO	1322	1266	1147	2069	-152	-107	771	C
ATOM	1430	CA	PRO	1322	4.078	8.523	38.436	1.00	11.63		C
ANISOU	1430	CA	PRO	1322	1189	1067	2162	-252	-204	350	C
ATOM	1431	CB	PRO	1322	4.003	7.095	39.017	1.00	15.58		C
ANISOU	1431	CB	PRO	1322	1730	1065	3123	-277	-639	557	C
ATOM	1432	CG	PRO	1322	4.456	7.263	40.447	1.00	15.69		C
ANISOU	1432	CG	PRO	1322	1544	1507	2912	-409	-475	1060	C
ATOM	1433	C	PRO	1322	2.739	9.235	38.500	1.00	11.20		C
ANISOU	1433	C	PRO	1322	1211	1119	1927	-222	-241	426	C
ATOM	1434	O	PRO	1322	1.962	9.020	37.570	1.00	12.81		O
ANISOU	1434	O	PRO	1322	1406	1443	2020	-85	-273	89	O
ATOM	1435	N	LYS	1323	2.450	10.021	39.534	1.00	10.65		N
ANISOU	1435	N	LYS	1323	988	1354	1705	-267	-37	485	N
ATOM	1436	CA	LYS	1323	1.184	10.764	39.595	1.00	12.28		C
ANISOU	1436	CA	LYS	1323	1085	1704	1876	-93	-219	380	C
ATOM	1437	CB	LYS	1323	0.593	10.863	40.987	1.00	15.93		C
ANISOU	1437	CB	LYS	1323	1821	1865	2365	-254	588	31	C
ATOM	1442	C	LYS	1323	1.469	12.162	39.063	1.00	12.40		C
ANISOU	1442	C	LYS	1323	1310	1508	1894	24	-242	227	C
ATOM	1443	O	LYS	1323	2.182	12.934	39.729	1.00	11.98		O
ANISOU	1443	O	LYS	1323	1356	1591	1604	-97	-17	198	O
ATOM	1444	N	ALA	1324	0.939	12.482	37.880	1.00	11.27		N
ANISOU	1444	N	ALA	1324	981	1505	1798	79	-103	231	N
ATOM	1445	CA	ALA	1324	1.272	13.747	37.248	1.00	11.18		C
ANISOU	1445	CA	ALA	1324	1262	1526	1462	-100	-94	96	C
ATOM	1446	CB	ALA	1324	0.424	13.928	35.982	1.00	11.94		C
ANISOU	1446	CB	ALA	1324	1319	1674	1543	-296	-244	129	C
ATOM	1447	C	ALA	1324	1.035	14.941	38.147	1.00	11.19		C
ANISOU	1447	C	ALA	1324	1053	1641	1557	-228	-67	-24	C
ATOM	1448	O	ALA	1324	1.830	15.903	38.165	1.00	11.22		O
ANISOU	1448	O	ALA	1324	1177	1371	1714	-102	-158	219	O
ATOM	1449	N	GLU	1325	-0.050	14.952	38.909	1.00	11.86		N
ANISOU	1449	N	GLU	1325	1005	1459	2041	192	90	264	N

Table 1 (continued)

ATOM	1450	CA	GLU	1325	-0.377	16.098	39.768	1.00	13.69		C
ANISOU	1450	CA	GLU	1325	1113	1567	2520	211	159	25	C
ATOM	1451	CB	GLU	1325	-1.831	15.883	40.233	1.00	17.24		C
ANISOU	1451	CB	GLU	1325	1083	2260	3207	187	431	-401	C
ATOM	1456	C	GLU	1325	0.635	16.276	40.879	1.00	13.70		C
ANISOU	1456	C	GLU	1325	1271	1598	2336	72	233	-65	C
ATOM	1457	O	GLU	1325	0.685	17.375	41.467	1.00	17.90		O
ANISOU	1457	O	GLU	1325	1520	1913	3370	170	-14	-547	O
ATOM	1458	N	MET	1326	1.454	15.287	41.216	1.00	12.21		N
ANISOU	1458	N	MET	1326	1168	1477	1995	-238	169	283	N
ATOM	1459	CA	MET	1326	2.418	15.414	42.307	1.00	11.67		C
ANISOU	1459	CA	MET	1326	1444	1436	1553	-328	326	251	C
ATOM	1460	CB	MET	1326	2.605	14.037	42.976	1.00	15.41		C
ANISOU	1460	CB	MET	1326	1916	1765	2174	-680	-197	724	C
ATOM	1461	CG	MET	1326	1.297	13.672	43.655	1.00	21.33		C
ANISOU	1461	CG	MET	1326	2606	2259	3238	-914	364	1411	C
ATOM	1462	SD	MET	1326	1.016	14.723	45.056	1.00	42.43		S
ANISOU	1462	SD	MET	1326	4873	6868	4382	-522	1952	-603	S
ATOM	1463	CE	MET	1326	1.072	13.580	46.440	1.00	72.67		C
ANISOU	1463	CE	MET	1326	12450	12012	3148	-6397	-96	1087	C
ATOM	1464	C	MET	1326	3.754	15.908	41.815	1.00	10.99		C
ANISOU	1464	C	MET	1326	1259	1416	1499	-217	148	166	C
ATOM	1465	O	MET	1326	4.663	16.137	42.611	1.00	13.71		O
ANISOU	1465	O	MET	1326	1504	2145	1560	-366	20	45	O
ATOM	1466	N	ARG	1327	3.918	16.079	40.498	1.00	9.88		N
ANISOU	1466	N	ARG	1327	1112	1186	1457	-149	139	187	N
ATOM	1467	CA	ARG	1327	5.145	16.649	39.965	1.00	9.45		C
ANISOU	1467	CA	ARG	1327	1081	1097	1414	-109	191	-53	C
ATOM	1468	CB	ARG	1327	5.193	16.418	38.449	1.00	9.35		C
ANISOU	1468	CB	ARG	1327	1252	941	1359	64	65	0	C
ATOM	1469	CG	ARG	1327	5.279	14.945	38.086	1.00	9.03		C
ANISOU	1469	CG	ARG	1327	1205	813	1414	-61	-303	69	C
ATOM	1470	CD	ARG	1327	5.273	14.706	36.548	1.00	8.86		C
ANISOU	1470	CD	ARG	1327	996	941	1428	6	-317	-4	C
ATOM	1471	NE	ARG	1327	4.902	13.295	36.410	1.00	9.09		N
ANISOU	1471	NE	ARG	1327	1098	958	1399	-60	-118	-52	N
ATOM	1472	CZ	ARG	1327	4.171	12.800	35.394	1.00	8.45		C
ANISOU	1472	CZ	ARG	1327	1106	860	1244	7	-138	-1	C
ATOM	1473	NH1	ARG	1327	3.757	13.543	34.369	1.00	8.64		N1+
ANISOU	1473	NH1	ARG	1327	1014	911	1357	183	-48	51	N1+
ATOM	1474	NH2	ARG	1327	3.882	11.505	35.429	1.00	9.00		N
ANISOU	1474	NH2	ARG	1327	1002	841	1575	0	-39	59	N
ATOM	1475	C	ARG	1327	5.180	18.125	40.263	1.00	8.46		C
ANISOU	1475	C	ARG	1327	1010	1092	1113	-23	-52	52	C
ATOM	1476	O	ARG	1327	4.138	18.778	40.332	1.00	10.53		O
ANISOU	1476	O	ARG	1327	1103	1088	1810	60	6	105	O
ATOM	1477	N	PRO	1328	6.341	18.733	40.403	1.00	8.99		N
ANISOU	1477	N	PRO	1328	1024	973	1418	23	-149	40	N
ATOM	1478	CD	PRO	1328	7.695	18.104	40.308	1.00	10.02		C
ANISOU	1478	CD	PRO	1328	1009	1033	1766	58	-168	132	C
ATOM	1479	CA	PRO	1328	6.404	20.170	40.675	1.00	9.59		C

Table 1 (continued)

ANISOU	1479	CA	PRO	1328	1136	971	1537	14	-184	40	C
ATOM	1480	CB	PRO	1328	7.905	20.445	40.874	1.00	11.74		C
ANISOU	1480	CB	PRO	1328	1172	1103	2185	-42	-211	-34	C
ATOM	1481	CG	PRO	1328	8.611	19.279	40.284	1.00	14.90		C
ANISOU	1481	CG	PRO	1328	1095	1444	3123	-178	78	-563	C
ATOM	1482	C	PRO	1328	5.903	20.993	39.494	1.00	9.40		C
ANISOU	1482	C	PRO	1328	1204	926	1443	-55	48	51	C
ATOM	1483	O	PRO	1328	5.979	20.570	38.344	1.00	11.20		O
ANISOU	1483	O	PRO	1328	1733	1113	1411	203	-127	26	O
ATOM	1484	N	SER	1329	5.398	22.192	39.797	1.00	8.90		N
ANISOU	1484	N	SER	1329	959	866	1556	-99	-22	38	N
ATOM	1485	CA	SER	1329	5.189	23.154	38.720	1.00	9.51		C
ANISOU	1485	CA	SER	1329	972	1064	1578	46	135	135	C
ATOM	1486	CB	SER	1329	4.347	24.325	39.215	1.00	10.36		C
ANISOU	1486	CB	SER	1329	870	1104	1963	107	23	12	C
ATOM	1487	OG	SER	1329	5.083	25.028	40.210	1.00	11.39		O
ANISOU	1487	OG	SER	1329	1047	1272	2010	77	144	-215	O
ATOM	1488	C	SER	1329	6.499	23.697	38.209	1.00	8.13		C
ANISOU	1488	C	SER	1329	856	879	1352	42	-74	26	C
ATOM	1489	O	SER	1329	7.547	23.638	38.880	1.00	8.32		O
ANISOU	1489	O	SER	1329	952	933	1274	45	-60	-24	O
ATOM	1490	N	PHE	1330	6.458	24.285	36.998	1.00	8.31		N
ANISOU	1490	N	PHE	1330	804	861	1492	38	-78	184	N
ATOM	1491	CA	PHE	1330	7.644	24.979	36.540	1.00	8.34		C
ANISOU	1491	CA	PHE	1330	893	909	1367	-124	-43	29	C
ATOM	1492	CB	PHE	1330	7.468	25.415	35.071	1.00	8.88		C
ANISOU	1492	CB	PHE	1330	1188	879	1308	10	28	-12	C
ATOM	1493	CG	PHE	1330	7.674	24.227	34.118	1.00	8.63		C
ANISOU	1493	CG	PHE	1330	973	815	1491	38	-73	-2	C
ATOM	1494	CD1	PHE	1330	8.916	23.623	33.985	1.00	8.74		C
ANISOU	1494	CD1	PHE	1330	1069	935	1316	184	-10	189	C
ATOM	1495	CD2	PHE	1330	6.617	23.734	33.371	1.00	8.48		C
ANISOU	1495	CD2	PHE	1330	1136	914	1173	-204	-102	205	C
ATOM	1496	CE1	PHE	1330	9.120	22.546	33.118	1.00	8.63		C
ANISOU	1496	CE1	PHE	1330	1275	795	1211	-16	-21	113	C
ATOM	1497	CE2	PHE	1330	6.788	22.659	32.489	1.00	9.18		C
ANISOU	1497	CE2	PHE	1330	1220	970	1297	-76	39	130	C
ATOM	1498	CZ	PHE	1330	8.052	22.079	32.374	1.00	9.20		C
ANISOU	1498	CZ	PHE	1330	1103	1052	1338	-133	9	332	C
ATOM	1499	C	PHE	1330	8.011	26.180	37.434	1.00	8.35		C
ANISOU	1499	C	PHE	1330	862	893	1416	15	-80	5	C
ATOM	1500	O	PHE	1330	9.191	26.494	37.549	1.00	8.94		O
ANISOU	1500	O	PHE	1330	927	1017	1452	-77	-106	-17	O
ATOM	1501	N	SER	1331	7.032	26.827	38.083	1.00	8.95		N
ANISOU	1501	N	SER	1331	997	947	1458	151	-23	62	N
ATOM	1502	CA	SER	1331	7.413	27.848	39.072	1.00	10.05		C
ANISOU	1502	CA	SER	1331	1209	1164	1445	-71	150	-122	C
ATOM	1503	CB	SER	1331	6.140	28.511	39.611	1.00	14.00		C
ANISOU	1503	CB	SER	1331	1207	1679	2434	386	72	-399	C
ATOM	1504	OG	SER	1331	5.497	29.274	38.624	1.00	20.39		O
ANISOU	1504	OG	SER	1331	2307	2271	3170	627	-286	79	O

Table 1 (continued)

ATOM	1505	C	SER	1331	8.248	27.284	40.207	1.00	9.10		C
ANISOU	1505	C	SER	1331	1064	1009	1385	-54	143	-244	C
ATOM	1506	O	SER	1331	9.250	27.877	40.592	1.00	9.80		O
ANISOU	1506	O	SER	1331	1049	923	1749	16	91	-208	O
ATOM	1507	N	GLU	1332	7.820	26.148	40.747	1.00	9.28		N
ANISOU	1507	N	GLU	1332	1065	957	1503	52	54	-176	N
ATOM	1508	CA	GLU	1332	8.616	25.507	41.796	1.00	9.73		C
ANISOU	1508	CA	GLU	1332	1137	1109	1452	24	115	-153	C
ATOM	1509	CB	GLU	1332	7.881	24.270	42.319	1.00	10.32		C
ANISOU	1509	CB	GLU	1332	1157	1239	1524	-133	191	-85	C
ATOM	1510	CG	GLU	1332	8.757	23.552	43.390	1.00	15.56		C
ANISOU	1510	CG	GLU	1332	1949	1811	2154	-114	-104	517	C
ATOM	1511	CD	GLU	1332	8.107	22.358	44.053	1.00	17.02		C
ANISOU	1511	CD	GLU	1332	2266	1867	2332	-276	-121	589	C
ATOM	1512	OE1	GLU	1332	6.885	22.139	43.922	1.00	23.13		O1-
ANISOU	1512	OE1	GLU	1332	2459	2653	3677	-929	-272	699	O1-
ATOM	1513	OE2	GLU	1332	8.806	21.599	44.736	1.00	24.46		O
ANISOU	1513	OE2	GLU	1332	3352	2542	3399	-454	-763	1449	O
ATOM	1514	C	GLU	1332	9.996	25.115	41.297	1.00	8.05		C
ANISOU	1514	C	GLU	1332	1019	785	1257	-115	8	-108	C
ATOM	1515	O	GLU	1332	11.011	25.264	41.978	1.00	9.15		O
ANISOU	1515	O	GLU	1332	1127	1090	1258	-157	-41	-28	O
ATOM	1516	N	LEU	1333	10.039	24.582	40.060	1.00	8.35		N
ANISOU	1516	N	LEU	1333	940	935	1297	-105	73	-135	N
ATOM	1517	CA	LEU	1333	11.339	24.192	39.520	1.00	7.78		C
ANISOU	1517	CA	LEU	1333	882	961	1113	-117	12	-112	C
ATOM	1518	CB	LEU	1333	11.145	23.464	38.167	1.00	8.52		C
ANISOU	1518	CB	LEU	1333	1207	780	1252	-8	-209	-218	C
ATOM	1519	CG	LEU	1333	10.493	22.077	38.311	1.00	8.18		C
ANISOU	1519	CG	LEU	1333	863	792	1451	77	-153	-145	C
ATOM	1520	CD1	LEU	1333	9.925	21.631	36.975	1.00	9.19		C
ANISOU	1520	CD1	LEU	1333	1204	830	1456	-25	-273	-204	C
ATOM	1521	CD2	LEU	1333	11.501	21.074	38.872	1.00	9.86		C
ANISOU	1521	CD2	LEU	1333	1184	893	1670	279	-190	-65	C
ATOM	1522	C	LEU	1333	12.263	25.374	39.336	1.00	7.37		C
ANISOU	1522	C	LEU	1333	881	844	1074	-32	-146	-85	C
ATOM	1523	O	LEU	1333	13.466	25.290	39.641	1.00	7.98		O
ANISOU	1523	O	LEU	1333	831	958	1242	31	-120	-212	O
ATOM	1524	N	VAL	1334	11.772	26.509	38.857	1.00	7.97		N
ANISOU	1524	N	VAL	1334	1034	794	1201	10	-184	-59	N
ATOM	1525	CA	VAL	1334	12.628	27.715	38.762	1.00	8.35		C
ANISOU	1525	CA	VAL	1334	1117	810	1244	-67	-190	-110	C
ATOM	1526	CB	VAL	1334	11.850	28.891	38.170	1.00	8.29		C
ANISOU	1526	CB	VAL	1334	1188	745	1217	-39	-232	-92	C
ATOM	1527	CG1	VAL	1334	12.602	30.211	38.360	1.00	9.62		C
ANISOU	1527	CG1	VAL	1334	1217	775	1663	-96	-19	-135	C
ATOM	1528	CG2	VAL	1334	11.575	28.593	36.689	1.00	8.88		C
ANISOU	1528	CG2	VAL	1334	1277	985	1112	-24	-25	-74	C
ATOM	1529	C	VAL	1334	13.172	28.074	40.130	1.00	7.99		C
ANISOU	1529	C	VAL	1334	898	909	1228	21	-163	-168	C
ATOM	1530	O	VAL	1334	14.351	28.374	40.294	1.00	8.68		O

Table 1 (continued)

ANISOU	1530	O	VAL	1334	948	970	1380	-21	-209	-158	O
ATOM	1531	N	SER	1335	12.293	28.068	41.153	1.00	8.46		N
ANISOU	1531	N	SER	1335	1111	868	1236	-14	-66	-147	N
ATOM	1532	CA	SER	1335	12.754	28.474	42.498	1.00	8.67		C
ANISOU	1532	CA	SER	1335	1018	1019	1256	39	-71	-214	C
ATOM	1533	CB	SER	1335	11.500	28.530	43.364	1.00	8.71		C
ANISOU	1533	CB	SER	1335	1005	1115	1189	38	-104	-248	C
ATOM	1534	OG	SER	1335	11.842	28.966	44.682	1.00	9.87		O
ANISOU	1534	OG	SER	1335	1275	1153	1322	-7	-124	-261	O
ATOM	1535	C	SER	1335	13.821	27.538	43.043	1.00	8.37		C
ANISOU	1535	C	SER	1335	1059	909	1213	58	-30	-123	C
ATOM	1536	O	SER	1335	14.892	27.964	43.502	1.00	9.11		O
ANISOU	1536	O	SER	1335	1132	1057	1274	46	-106	-252	O
ATOM	1537	N	ARG	1336	13.565	26.206	42.983	1.00	8.62		N
ANISOU	1537	N	ARG	1336	1028	990	1256	3	26	-78	N
ATOM	1538	CA	ARG	1336	14.515	25.252	43.542	1.00	8.14		C
ANISOU	1538	CA	ARG	1336	1174	809	1111	55	56	-84	C
ATOM	1539	CB	ARG	1336	13.921	23.834	43.582	1.00	9.71		C
ANISOU	1539	CB	ARG	1336	1206	974	1509	-146	-6	-19	C
ATOM	1540	CG	ARG	1336	12.764	23.699	44.580	1.00	12.51		C
ANISOU	1540	CG	ARG	1336	1203	1574	1976	-295	277	-168	C
ATOM	1541	CD	ARG	1336	12.324	22.240	44.632	1.00	16.53		C
ANISOU	1541	CD	ARG	1336	1965	1828	2489	-794	39	224	C
ATOM	1542	NE	ARG	1336	11.333	22.000	45.675	1.00	20.55		N
ANISOU	1542	NE	ARG	1336	2059	2710	3039	-569	188	1093	N
ATOM	1543	CZ	ARG	1336	11.602	21.702	46.960	1.00	21.12		C
ANISOU	1543	CZ	ARG	1336	2246	2809	2969	-365	349	1111	C
ATOM	1544	NH1	ARG	1336	12.880	21.604	47.379	1.00	19.31		N1+
ANISOU	1544	NH1	ARG	1336	2479	2424	2434	70	177	-32	N1+
ATOM	1545	NH2	ARG	1336	10.658	21.501	47.831	1.00	24.03		N
ANISOU	1545	NH2	ARG	1336	2743	3291	3098	-790	663	678	N
ATOM	1546	C	ARG	1336	15.809	25.197	42.747	1.00	7.85		C
ANISOU	1546	C	ARG	1336	947	829	1206	-6	-140	-86	C
ATOM	1547	O	ARG	1336	16.875	25.093	43.338	1.00	8.97		O
ANISOU	1547	O	ARG	1336	1131	988	1290	35	-222	-136	O
ATOM	1548	N	ILE	1337	15.719	25.260	41.407	1.00	8.03		N
ANISOU	1548	N	ILE	1337	979	916	1157	8	-40	-62	N
ATOM	1549	CA	ILE	1337	16.961	25.203	40.635	1.00	8.17		C
ANISOU	1549	CA	ILE	1337	1048	857	1199	-46	-48	-85	C
ATOM	1550	CB	ILE	1337	16.650	24.826	39.184	1.00	8.43		C
ANISOU	1550	CB	ILE	1337	851	1154	1197	-104	-87	-203	C
ATOM	1551	CG2	ILE	1337	17.917	24.873	38.322	1.00	9.76		C
ANISOU	1551	CG2	ILE	1337	1010	1299	1397	61	125	-169	C
ATOM	1552	CG1	ILE	1337	15.973	23.446	39.108	1.00	8.62		C
ANISOU	1552	CG1	ILE	1337	1048	956	1272	-49	-250	-84	C
ATOM	1553	CD1	ILE	1337	15.426	23.048	37.743	1.00	9.65		C
ANISOU	1553	CD1	ILE	1337	1196	1200	1269	-13	-275	-167	C
ATOM	1554	C	ILE	1337	17.710	26.518	40.769	1.00	8.27		C
ANISOU	1554	C	ILE	1337	842	1093	1209	-55	-168	-302	C
ATOM	1555	O	ILE	1337	18.946	26.487	40.759	1.00	9.46		O
ANISOU	1555	O	ILE	1337	937	1178	1477	-60	-192	-228	O

Table 1 (continued)

ATOM	1556	N	SER	1338	17.043	27.673	40.942	1.00	8.80		N
ANISOU	1556	N	SER	1338	1158	818	1369	-118	-97	-139	N
ATOM	1557	CA	SER	1338	17.794	28.895	41.258	1.00	9.19		C
ANISOU	1557	CA	SER	1338	1192	1059	1239	-250	-265	-207	C
ATOM	1558	CB	SER	1338	16.805	30.044	41.512	1.00	11.88		C
ANISOU	1558	CB	SER	1338	1456	600	2456	-125	-936	-2	C
ATOM	1559	OG	SER	1338	16.175	30.499	40.359	1.00	12.96		O
ANISOU	1559	OG	SER	1338	1425	1736	1763	121	-183	-133	O
ATOM	1560	C	SER	1338	18.651	28.684	42.483	1.00	8.30		C
ANISOU	1560	C	SER	1338	949	923	1281	57	-129	-157	C
ATOM	1561	O	SER	1338	19.817	29.078	42.554	1.00	9.12		O
ANISOU	1561	O	SER	1338	951	1164	1350	-80	-120	-211	O
ATOM	1562	N	ALA	1339	18.054	28.055	43.517	1.00	8.47		N
ANISOU	1562	N	ALA	1339	1041	886	1291	-27	-135	-155	N
ATOM	1563	CA	ALA	1339	18.793	27.824	44.748	1.00	8.28		C
ANISOU	1563	CA	ALA	1339	984	980	1180	-13	-59	-189	C
ATOM	1564	CB	ALA	1339	17.856	27.267	45.821	1.00	8.73		C
ANISOU	1564	CB	ALA	1339	1004	936	1377	-120	-30	-137	C
ATOM	1565	C	ALA	1339	19.967	26.898	44.500	1.00	8.40		C
ANISOU	1565	C	ALA	1339	1104	1079	1008	64	-60	-194	C
ATOM	1566	O	ALA	1339	21.086	27.149	44.966	1.00	9.08		O
ANISOU	1566	O	ALA	1339	1042	1075	1334	144	-161	-198	O
ATOM	1567	N	ILE	1340	19.769	25.774	43.778	1.00	8.62		N
ANISOU	1567	N	ILE	1340	1053	956	1268	60	15	-132	N
ATOM	1568	CA	ILE	1340	20.908	24.859	43.501	1.00	8.91		C
ANISOU	1568	CA	ILE	1340	953	830	1603	-52	-57	-196	C
ATOM	1569	CB	ILE	1340	20.360	23.612	42.790	1.00	9.84		C
ANISOU	1569	CB	ILE	1340	1108	939	1693	-89	-120	-286	C
ATOM	1570	CG2	ILE	1340	21.495	22.740	42.277	1.00	11.36		C
ANISOU	1570	CG2	ILE	1340	1209	1087	2020	109	58	-330	C
ATOM	1571	CG1	ILE	1340	19.390	22.847	43.725	1.00	10.23		C
ANISOU	1571	CG1	ILE	1340	1134	1089	1665	-271	-136	-146	C
ATOM	1572	CD1	ILE	1340	18.582	21.793	42.957	1.00	11.89		C
ANISOU	1572	CD1	ILE	1340	1440	1024	2054	-303	-389	-101	C
ATOM	1573	C	ILE	1340	21.993	25.550	42.717	1.00	8.90		C
ANISOU	1573	C	ILE	1340	955	1003	1425	19	-60	-112	C
ATOM	1574	O	ILE	1340	23.189	25.477	43.049	1.00	9.92		O
ANISOU	1574	O	ILE	1340	907	1113	1750	37	-109	-204	O
ATOM	1575	N	PHE	1341	21.630	26.255	41.661	1.00	9.18		N
ANISOU	1575	N	PHE	1341	1280	931	1277	-76	-117	-186	N
ATOM	1576	CA	PHE	1341	22.575	27.011	40.839	1.00	8.83		C
ANISOU	1576	CA	PHE	1341	1001	1117	1239	-23	-54	-175	C
ATOM	1577	CB	PHE	1341	21.766	27.812	39.822	1.00	9.26		C
ANISOU	1577	CB	PHE	1341	887	1351	1282	84	46	-18	C
ATOM	1578	CG	PHE	1341	22.540	28.818	38.967	1.00	9.61		C
ANISOU	1578	CG	PHE	1341	1053	1261	1338	-61	24	-105	C
ATOM	1579	CD1	PHE	1341	23.266	28.379	37.890	1.00	8.96		C
ANISOU	1579	CD1	PHE	1341	797	1429	1179	-207	-69	-84	C
ATOM	1580	CD2	PHE	1341	22.508	30.172	39.267	1.00	13.06		C
ANISOU	1580	CD2	PHE	1341	1834	1322	1805	-158	118	-291	C
ATOM	1581	CE1	PHE	1341	23.944	29.286	37.086	1.00	10.76		C

Table 1 (continued)

ANISOU	1581	CE1	PHE	1341	1084	1407	1597	-353	72	-86	C
ATOM	1582	CE2	PHE	1341	23.192	31.085	38.470	1.00	15.09		C
ANISOU	1582	CE2	PHE	1341	2304	1223	2207	-114	328	-97	C
ATOM	1583	CZ	PHE	1341	23.931	30.632	37.367	1.00	12.84		C
ANISOU	1583	CZ	PHE	1341	1360	1371	2148	-262	26	-126	C
ATOM	1584	C	PHE	1341	23.437	27.920	41.680	1.00	8.75		C
ANISOU	1584	C	PHE	1341	880	1117	1325	38	-16	-213	C
ATOM	1585	O	PHE	1341	24.638	28.059	41.449	1.00	11.08		O
ANISOU	1585	O	PHE	1341	991	1716	1503	-95	-44	-418	O
ATOM	1586	N	SER	1342	22.829	28.583	42.663	1.00	8.78		N
ANISOU	1586	N	SER	1342	1073	929	1333	-47	-64	-167	N
ATOM	1587	CA	SER	1342	23.508	29.588	43.467	1.00	9.79		C
ANISOU	1587	CA	SER	1342	1025	1195	1499	173	-200	-453	C
ATOM	1588	CB	SER	1342	22.473	30.329	44.315	1.00	9.78		C
ANISOU	1588	CB	SER	1342	984	1144	1586	6	89	-299	C
ATOM	1589	OG	SER	1342	22.068	29.572	45.430	1.00	10.05		O
ANISOU	1589	OG	SER	1342	1176	1176	1466	9	-97	-311	O
ATOM	1590	C	SER	1342	24.570	29.011	44.379	1.00	9.61		C
ANISOU	1590	C	SER	1342	990	1195	1468	19	-95	-305	C
ATOM	1591	O	SER	1342	25.340	29.795	44.964	1.00	11.23		O
ANISOU	1591	O	SER	1342	1090	1252	1926	98	-301	-565	O
ATOM	1592	N	THR	1343	24.632	27.692	44.525	1.00	10.45		N
ANISOU	1592	N	THR	1343	1217	1125	1629	252	-347	-428	N
ATOM	1593	CA	THR	1343	25.600	27.078	45.464	1.00	12.07		C
ANISOU	1593	CA	THR	1343	1479	1389	1720	330	-356	-346	C
ATOM	1594	CB	THR	1343	25.000	25.891	46.215	1.00	13.04		C
ANISOU	1594	CB	THR	1343	1907	1482	1564	405	-143	-273	C
ATOM	1595	OG1	THR	1343	24.737	24.803	45.298	1.00	12.76		O
ANISOU	1595	OG1	THR	1343	1902	1281	1666	228	104	-227	O
ATOM	1596	CG2	THR	1343	23.671	26.281	46.888	1.00	14.32		C
ANISOU	1596	CG2	THR	1343	2133	1470	1839	513	153	-243	C
ATOM	1597	C	THR	1343	26.881	26.637	44.743	1.00	12.17		C
ANISOU	1597	C	THR	1343	1296	1324	2004	355	-363	-488	C
ATOM	1598	O	THR	1343	27.719	26.095	45.468	1.00	16.07		O
ANISOU	1598	O	THR	1343	1607	2231	2267	571	-656	-419	O
ATOM	1599	N	PHE	1344	26.990	26.884	43.459	1.00	12.84		N
ANISOU	1599	N	PHE	1344	1367	1612	1900	399	-269	-609	N
ATOM	1600	CA	PHE	1344	28.203	26.534	42.732	1.00	14.34		C
ANISOU	1600	CA	PHE	1344	1457	1713	2279	145	-27	-685	C
ATOM	1601	CB	PHE	1344	27.848	25.821	41.403	1.00	12.78		C
ANISOU	1601	CB	PHE	1344	1671	1415	1769	121	173	-242	C
ATOM	1602	CG	PHE	1344	27.345	24.421	41.768	1.00	12.51		C
ANISOU	1602	CG	PHE	1344	1419	1411	1922	200	-55	-344	C
ATOM	1603	CD1	PHE	1344	26.058	24.180	42.147	1.00	11.90		C
ANISOU	1603	CD1	PHE	1344	1258	1760	1502	-53	-320	-351	C
ATOM	1604	CD2	PHE	1344	28.280	23.369	41.721	1.00	16.99		C
ANISOU	1604	CD2	PHE	1344	1844	1427	3185	402	306	-412	C
ATOM	1605	CE1	PHE	1344	25.675	22.898	42.499	1.00	14.59		C
ANISOU	1605	CE1	PHE	1344	1722	1904	1917	-105	-144	-149	C
ATOM	1606	CE2	PHE	1344	27.903	22.099	42.055	1.00	16.79		C
ANISOU	1606	CE2	PHE	1344	1979	1475	2924	202	-167	-261	C

Table 1 (continued)

ATOM	1607	CZ	PHE	1344	26.589	21.858	42.445	1.00	18.76		C
ANISOU	1607	CZ	PHE	1344	2055	1812	3261	54	-85	-59	C
ATOM	1608	C	PHE	1344	29.076	27.730	42.403	1.00	16.20		C
ANISOU	1608	C	PHE	1344	1183	1677	3296	218	-113	-754	C
ATOM	1609	O	PHE	1344	28.612	28.821	42.162	1.00	17.22		O
ANISOU	1609	O	PHE	1344	1411	1670	3463	140	-108	-621	O
ATOM	1610	N	ILE	1345	30.381	27.445	42.380	1.00	22.23		N
ANISOU	1610	N	ILE	1345	1104	2594	4750	315	-203	-1085	N
ATOM	1611	CA	ILE	1345	31.333	28.468	41.923	1.00	28.36		C
ANISOU	1611	CA	ILE	1345	1120	4707	4948	-359	-345	-102	C
ATOM	1612	CB	ILE	1345	32.700	28.401	42.600	1.00	31.48		C
ANISOU	1612	CB	ILE	1345	1667	4345	5949	-490	-1170	88	C
ATOM	1613	CG2	ILE	1345	33.702	29.326	41.922	1.00	34.84		C
ANISOU	1613	CG2	ILE	1345	1562	4401	7275	-865	-408	-940	C
ATOM	1614	CG1	ILE	1345	32.633	28.692	44.101	1.00	34.37		C
ANISOU	1614	CG1	ILE	1345	2059	5080	5918	1032	-1654	23	C
ATOM	1615	CD1	ILE	1345	32.799	27.504	45.004	1.00	44.90		C
ANISOU	1615	CD1	ILE	1345	8417	3416	5227	1404	551	-776	C
ATOM	1616	C	ILE	1345	31.429	28.229	40.435	1.00	32.47		C
ANISOU	1616	C	ILE	1345	743	6497	5099	-143	-91	-505	C
ATOM	1617	O	ILE	1345	31.574	27.091	39.970	1.00	52.32		O
ANISOU	1617	O	ILE	1345	4633	7954	7293	636	-439	-2761	O
ATOM	1618	N	GLY	1346	31.341	29.233	39.579	1.00	42.18		N
ANISOU	1618	N	GLY	1346	1564	9187	5276	-737	634	1205	N
ATOM	1619	CA	GLY	1346	31.358	28.702	38.197	1.00	42.04		C
ANISOU	1619	CA	GLY	1346	1993	8390	5590	-288	605	829	C
ATOM	1620	C	GLY	1346	32.744	28.804	37.605	1.00	35.42		C
ANISOU	1620	C	GLY	1346	2009	5733	5715	-1032	594	-588	C
ATOM	1621	O	GLY	1346	32.847	29.466	36.570	1.00	29.91		O
ANISOU	1621	O	GLY	1346	2517	3128	5720	-609	1243	-1467	O
ATOM	1622	N	GLU	1347	33.764	28.197	38.202	1.00	32.42		N
ANISOU	1622	N	GLU	1347	1855	5078	5384	-1023	711	-1174	N
ATOM	1623	CA	GLU	1347	35.102	28.380	37.583	1.00	34.52		C
ANISOU	1623	CA	GLU	1347	2028	4846	6242	-1021	1233	-2503	C
ATOM	1624	CB	GLU	1347	35.866	29.445	38.387	1.00	43.54		C
ANISOU	1624	CB	GLU	1347	3110	5574	7859	-2136	1159	-2882	C
ATOM	1625	CG	GLU	1347	35.257	30.837	38.232	1.00	50.27		C
ANISOU	1625	CG	GLU	1347	6099	5049	7952	-2109	975	-2900	C
ATOM	1626	CD	GLU	1347	36.216	31.880	38.781	1.00	59.94		C
ANISOU	1626	CD	GLU	1347	7531	5502	9744	-3279	-210	-1829	C
ATOM	1627	OE1	GLU	1347	36.704	31.654	39.911	1.00	72.63		O1-
ANISOU	1627	OE1	GLU	1347	7542	9402	10654	-3681	-1627	-1956	O1-
ATOM	1628	OE2	GLU	1347	36.456	32.885	38.078	1.00	80.71		O
ANISOU	1628	OE2	GLU	1347	11428	5956	13280	-4260	612	-625	O
ATOM	1629	C	GLU	1347	35.836	27.076	37.524	1.00	28.47		C
ANISOU	1629	C	GLU	1347	2371	5024	3423	-637	340	-1363	C
ATOM	1630	O	GLU	1347	35.699	26.251	38.444	1.00	53.72		O
ANISOU	1630	O	GLU	1347	6352	8133	5926	730	3277	1242	O
ATOM	1631	N	HIS	1348	36.626	26.832	36.477	1.00	25.55		N
ANISOU	1631	N	HIS	1348	2319	4355	3034	57	52	-915	N
ATOM	1632	CA	HIS	1348	37.487	25.676	36.508	1.00	26.15		C

Table 1 (continued)

ANISOU	1632	CA	HIS	1348	2947	4334	2655	266	-231	-331	C
ATOM	1633	CB	HIS	1348	37.827	25.311	35.067	1.00	22.43		C
ANISOU	1633	CB	HIS	1348	1406	4322	2793	354	-114	-334	C
ATOM	1634	CG	HIS	1348	36.654	24.757	34.330	1.00	20.85		C
ANISOU	1634	CG	HIS	1348	1777	3333	2813	198	-534	199	C
ATOM	1635	CD2	HIS	1348	36.160	25.236	33.166	1.00	19.00		C
ANISOU	1635	CD2	HIS	1348	1957	2715	2549	-26	-196	149	C
ATOM	1636	ND1	HIS	1348	35.884	23.661	34.703	1.00	20.19		N
ANISOU	1636	ND1	HIS	1348	2566	2754	2353	394	-601	190	N
ATOM	1637	CE1	HIS	1348	34.960	23.526	33.759	1.00	20.25		C
ANISOU	1637	CEI	HIS	1348	2253	3002	2438	-199	-437	528	C
ATOM	1638	NE2	HIS	1348	35.105	24.478	32.810	1.00	14.15		N
ANISOU	1638	NE2	HIS	1348	1278	2111	1989	507	69	-48	N
ATOM	1639	C	HIS	1348	38.785	25.887	37.281	1.00	26.98		C
ANISOU	1639	C	HIS	1348	3381	3635	3237	291	-787	-522	C
ATOM	1640	O	HIS	1348	39.511	24.880	37.403	1.00	32.17		O
ANISOU	1640	O	HIS	1348	3862	3955	4406	527	-1046	318	O
ATOM	1641	OXT	HIS	1348	39.104	27.002	37.772	1.00	29.89		O1-
ANISOU	1641	OXT	HIS	1348	2610	4203	4545	-784	1366	-1301	O1-
ANISOU	2307	C01	AGI	1	1424	1244	1271	107	-113	-8	
ATOM	2308	C02	AGI	1	17.248	25.870	14.705	1.00	11.23		
ANISOU	2308	C02	AGI	1	1593	1288	1385	27	17	-42	
ATOM	2309	C03	AGI	1	19.270	27.557	14.359	1.00	11.18		
ANISOU	2309	C03	AGI	1	1576	1385	1288	-25	177	-76	
ATOM	2310	C04	AGI	1	17.142	28.281	14.903	1.00	10.33		
ANISOU	2310	C04	AGI	I	1425	1264	1237	144	-269	177	
ATOM	2311	C05	AGI	1	15.862	25.858	14.999	1.00	11.47		
ANISOU	2311	C05	AGI	1	1622	1302	1432	-11	124	112	
ATOM	2312	S06	AGI	1	17.786	24.273	14.417	1.00	11.85		
ANISOU	2312	S06	AGI	1	1760	1225	1516	96	-40	0	
ATOM	2313	C07	AGI	1	19.293	28.958	14.483	1.00	11.57		
ANISOU	2313	C07	AGI	1	1529	1400	1469	-68	-229	-9	
ATOM	2314	C08	AGI	1	20.378	26.774	14.112	1.00	11.98		
ANISOU	2314	C08	AGI	1	1525	1600	1427	-3	111	-103	
ATOM	2315	N09	AGI	1	18.016	29.358	14.779	1.00	11.45		
ANISOU	2315	N09	AGI	1	1554	1301	1494	-37	-190	39	
ATOM	2316	C10	AGI	1	15.805	28.308	15.186	1.00	11.35		
ANISOU	2316	C10	AGI	1	1301	1327	1685	152	-337	-83	
ATOM	2317	C11	AGI	1	15.114	27.013	15.245	1.00	12.38		
ANISOU	2317	C11	AGI	1	1642	1380	1681	97	25	248	
ATOM	2318	N12	AGI	1	15.327	24.561	15.035	1.00	11.68		
ANISOU	2318	N12	AGI	1	1728	1354	1354	-82	-90	87	
ATOM	2319	C13	AGI	1	16.275	23.604	14.744	1.00	11.95		
ANISOU	2319	C13	AGI	1	1869	1304	1369	39	34	202	
ATOM	2320	O14	AGI	1	20.237	29.724	14.301	1.00	12.24		
ANISOU	2320	014	AGI	1	1692	1416	1543	-150	-48	-32	
ATOM	2321	N15	AGI	1	21.614	27.359	14.247	1.00	12.75		
AMSOU	2321	N15	AGI	1	1500	1840	1505	50	-316	68	
ATOM	2322	C16	AGI	1	22.834	26.782	14.157	1.00	13.67		
ANISOU	2322	C16	AGI	1	1563	1910	1719	27	45	-28	
ATOM	2323	C17	AGI	1	23.956	27.612	14.114	1.00	15.83		

Table 1 (continued)

ANISOU	2323	C17	AGI	1	1525	2253	2238	-23	258	-252	
ATOM	2324	C18	AGI	1	22.982	25.380	14.099	1.00	14.95		
ANISOU	2324	C18	AGI	1	2103	1915	1661	270	427	225	
ATOM	2325	C19	AGI	1	25.237	27.058	14.005	1.00	20.32		
ANISOU	2325	C19	AGI	1	1709	2588	3424	97	966	-237	
ATOM	2326	C20	AGI	1	24.272	24.821	14.031	1.00	16.85		
ANISOU	2326	C20	AGI	1	2237	2209	1955	445	278	366	
ATOM	2327	C21	AGI	1	25.399	25.679	13.982	1.00	20.28		
ANISOU	2327	C21	AGI	1	2047	2603	3057	394	453	-424	
ATOM	2328	S22	AGI	1	26.986	25.032	13.876	1.00	26.64		
ANISOU	2328	S22	AGI	1	2226	3468	4428	811	678	-405	
ATOM	2329	N23	AGI	1	27.676	24.971	15.376	1.00	37.62		
ANISOU	2329	N23	AGI	1	3078	6437	4778	2628	83	-81	
ATOM	2330	024	AGI	1	26.827	23.716	13.311	1.00	38.19		
ANISOU	2330	024	AGI	1	2627	3738	8146	1100	929	-1697	
ATOM	2331	025	AGI	1	27.805	25.956	13.104	1.00	33.13		
ANISOU	2331	025	AGI	1	2234	4778	5575	567	1078	291	
ATOM	2332	C26	AGI	1	27.374	25.661	16.611	1.00	37.52		
ANISOU	2332	C26	AGI	1	2405	7263	4586	-168	385	-695	
ATOM	2281	C2	PG1	2	27.637	9.800	25.901	1.00	46.69		
ANISOU	2281	C2	PG1	2	1814	7160	8766	-1009	845	-92	
ATOM	2282	C1	PG1	2	26.998	8.769	23.869	1.00	59.49		
ANISOU	2282	C1	PG1	2	4296	8204	10103	-1026	2989	-3292	
ATOM	2283	O1	PG1	2	27.655	9.872	24.485	1.00	49.46		
ANISOU	2283	O1	PG1	2	2873	7162	8759	-1022	848	-278	
ATOM	2284	02	PG1	2	27.875	12.238	25.632	1.00	51.26		
ANISOU	2284	02	PG1	2	4605	7234	7637	-1392	589	128	
ATOM	2285	C3	PG1	2	27.920	11.164	26.550	1.00	49.75		
ANISOU	2285	C3	PG1	2	3707	6963	8231	-940	745	211	
ATOM	2286	C4	PG1	2	28.756	13.287	25.910	1.00	45.26		
ANISOU	2286	C4	PG1	2	4805	6323	6069	-685	666	-509	
ATOM	2287	C5	PG1	2	29.745	13.688	24.814	1.00	34.91		
ANISOU	2287	C5	PG1	2	3413	4955	4898	-386	-479	-793	
ATOM	2288	03	PG1	2	30.945	14.190	25.383	1.00	27.74		
ANISOU	2288	03	PG1	2	3717	3007	3816	462	-1260	173	
ATOM	2289	C6	PG1	2	30.959	15.543	25.802	1.00	24.64		
ANISOU	2289	C6	PG1	2	2986	2888	3489	296	10	477	
ATOM	2290	C7	PG1	2	32.356	15.754	26.470	1.00	23.41		
ANISOU	2290	C7	PG1	2	3219	2502	3172	101	-17	354	
ATOM	2291	04	PG1	2	32.155	15.013	27.651	1.00	21.96		
ANISOU	2291	04	PG1	2	3477	2139	2726	202	130	-176	
ATOM	2292	C8	PG1	2	33.232	15.202	28.546	1.00	20.10		
ANISOU	2292	C8	PG1	2	3199	2158	2279	-79	494	-644	
ATOM	2293	C9	PG1	2	32.923	14.316	29.745	1.00	17.08		
ANISOU	2293	C9	PG1	2	1939	1779	2771	-370	-3	-461	
ATOM	2294	05	PG1	2	31.849	14.964	30.452	1.00	17.87		
ANISOU	2294	O5	PG1	2	2368	1615	2808	-140	471	62	
ATOM	2295	C10	PG1	2	31.399	14.106	31.468	1.00	18.56		
ANISOU	2295	C10	PG1	2	2715	1343	2995	-66	392	161	
ATOM	2296	C11	PG1	2	30.157	14.741	32.112	1.00	16.59		
ANISOU	2296	C11	PG1	2	2182	1720	2403	-471	118	-26	

Table 1 (continued)

	ATOM	2297	06	PG1	2	30.606	15.974	32.662	1.00	14.00		
	ANISOU	2297	06	PG1	2	1519	1675	2125	-156	-121	0	
	ATOM	2298	C12	PG1	2	29.527	16.652	33.314	1.00	13.38		
	ANISOU	2298	C12	PG1	2	1286	2016	1780	-251	110	217	
	ATOM	2299	C13	PG1	2	30.169	17.824	34.055	1.00	13.84		
	ANISOU	2299	C13	PG1	2	1830	1577	1853	3	186	239	
	ATOM	2300	07	PG1	2	30.650	18.743	33.089	1.00	12.58		
	ANISOU	2300	07	PG1	2	1441	1537	1802	112	13	189	
	ATOM	2301	C14	PG1	2	31.063	19.989	33.621	1.00	13.08		
	ANISOU	2301	C14	PG1	2	1459	1447	2063	131	-181	62	
	ATOM	2302	C15	PG1	2	32.293	19.915	34.567	1.00	13.72		
	ANISOU	2302	C15	PG1	2	1383	1975	1853	208	-77	126	
	ATOM	2303	O8	PG1	2	33.387	19.425	33.786	1.00	12.82		
	ANISOU	2303	08	PG1	2	1453	1668	1751	116	27	224	
	ATOM	2304	C16	PG1	2	34.515	18.933	34.533	1.00	20.74		
	ANISOU	2304	C16	PG1	2	1780	3687	2413	1089	122	593	
	ATOM	2305	C17	PG1	2	35.616	18.454	33.843	1.00	23.49		
	ANISOU	2305	C17	PG1	2	1639	3602	3684	743	777	638	
	ATOM	2306	09	PG1	2	36.710	19.364	33.366	1.00	20.22		
	ANISOU	2306	09	PG1	2	2338	2854	2489	508	381	411	
	ATOM	2271	C6	PG2	3	6.745	15.876	15.090	1.00	34.33		
	ANISOU	2271	C6	PG2	3	3183	6730	3133	1454	128	857	
	ATOM	2272	C7	PG2	3	7.219	15.032	16.319	1.00	25.66		
	ANISOU	2272	C7	PG2	3	2175	4321	3254	456	655	755	
	ATOM	2273	04	PG2	3	6.470	15.437	17.428	1.00	22.57		
	ANISOU	2273	04	PG2	3	2271	3181	3125	785	167	497	
	ATOM	2274	C8	PG2	3	6.764	14.842	18.666	1.00	17.33		
	ANISOU	2274	C8	PG2	3	1970	1841	2774	275	-316	-190	
	ATOM	2275	C9	PG2	3	5.683	15.202	19.699	1.00	18.90		
	ANISOU	2275	C9	PG2	3	2088	2289	2802	-96	-201	-336	
	ATOM	2276	O5	PG2	3	4.466	14.508	19.358	1.00	17.83		
	ANISOU	2276	05	PG2	3	2201	2137	2435	-230	-196	59	
	ATOM	2277	C10	PG2	3	3.424	14.900	20.248	1.00	20.16		
	ANISOU	2277	C10	PG2	3	2113	2721	2826	76	-159	-131	
	ATOM	2278	C11	PG2	3	2.085	14.250	19.824	1.00	23.43		
	ANISOU	2278	C11	PG2	3	2333	3640	2930	-505	139	-119	
	ATOM	2279	06	PG2	3	1.801	14.745	18.491	1.00	24.28		
	ANISOU	2279	06	PG2	3	2519	3696	3012	-374	-480	-368	
	ATOM	2280	C12	PG2	3	0.634	14.086	17.988	1.00	26.84		
	ANISOU	2280	C12	PG2	3	2909	4233	3055	-1421	45	-373	
	ATOM	2338	OH2	HOH	2001	16.059	36.368	20.087	1.00	30.04		
	ANISOU	2338	OH2	HOH	2001	3422	3777	4215	-1746	418	47	
	ATOM	2339	OH2	HOH	2002	3.991	24.550	35.564	1.00	13.01		
	ANISOU	2339	OH2	HOH	2002	1244	2095	1606	247	-209	207	
	ATOM	2340	OH2	HOH	2003	-1.459	12.785	29.750	1.00	14.50		
	ANISOU	2340	OH2	HOH	2003	1560	1941	2010	171	-329	-71	
	ATOM	2341	OH2	HOH	2004	23.419	6.044	30.575	1.00	18.48		
	ANISOU	2341	OH2	HOH	2004	1950	2339	2732	418	-129	-49	
	ATOM	2342	OH2	HOH	2005	9.610	30.646	40.439	1.00	11.74		
	ANISOU	2342	OH2	HOH	2005	1512	1159	1788	-73	57	-136	
	ATOM	2343	OH2	HOH	2006	7.713	17.830	26.517	1.00	8.88		

Table 1 (continued)

ANISOU	2343	OH2	HOH	2006	1017	998	1358	70	-139	28	
ATOM	2344	OH2	HOH	2007	17.870	16.008	23.308	1.00	9.47		
ANISOU	2344	OH2	HOH	2007	1359	955	1286	104	-189	11	
ATOM	2345	OH2	HOH	2008	21.105	13.556	25.188	1.00	10.04		
ANISOU	2345	OH2	HOH	2008	1115	1275	1425	201	145	-1	
ATOM	2346	OH2	HOH	2009	11.978	27.393	46.893	1.00	12.79		
ANISOU	2346	OH2	HOH	2009	2177	1306	1377	53	-67	-307	
ATOM	2347	OH2	HOH	2010	3.593	23.317	29.486	1.00	10.67		
ANISOU	2347	OH2	HOH	2010	1035	1088	1932	12	-67	-134	
ATOM	2348	OH2	HOH	2011	2.119	22.469	36.569	1.00	17.30		
ANISOU	2348	OH2	HOH	2011	2414	2016	2143	137	-357	141	
ATOM	2349	OH2	HOH	2012	4.387	16.752	27.179	1.00	9.09		
ANISOU	2349	OH2	HOH	2012	1048	1035	1369	-34	-174	29	
ATOM	2350	OH2	HOH	2013	13.856	8.307	34.680	1.00	9.66		
ANISOU	2350	OH2	HOH	2013	1010	1057	1605	69	-39	-95	
ATOM	2351	OH2	HOH	2014	5.073	12.687	27.611	1.00	10.04		
ANISOU	2351	OH2	HOH	2014	1287	1057	1471	154	-150	49	
ATOM	2352	OH2	HOH	2015	-2.674	28.202	25.274	1.00	19.18		
ANISOU	2352	OH2	HOH	2015	2267	2160	2860	-20	-424	280	
ATOM	2353	OH2	HOH	2016	9.576	34.588	22.992	1.00	14.31		
ANISOU	2353	OH2	HOH	2016	2070	1592	1774	564	-448	-324	
ATOM	2354	OH2	HOH	2017	6.335	21.231	20.029	1.00	15.09		
ANISOU	2354	OH2	HOH	2017	1538	2538	1658	-411	-233	287	
ATOM	2355	OH2	HOH	2018	6.469	15.014	27.130	1.00	9.55		
ANISOU	2355	OH2	HOH	2018	1121	1016	1493	-27	-329	-188	
ATOM	2356	OH2	HOH	2019	7.840	14.394	24.898	1.00	10.08		
ANISOU	2356	OH2	HOH	2019	1286	996	1547	-121	-34	-133	
ATOM	2357	OH2	HOH	2020	27.816	13.613	35.155	1.00	12.76		
ANISOU	2357	OH2	HOH	2020	1454	1523	1872	-58	127	315	
ATOM	2358	OH2	HOH	2021	10.551	15.115	24.202	1.00	10.23		
ANISOU	2358	OH2	HOH	2021	1239	842	1806	-20	-55	11	
ATOM	2359	OH2	HOH	2022	18.390	13.963	21.493	1.00	10.05		
ANISOU	2359	OH2	HOH	2022	1223	1093	1501	-18	-110	-121	
ATOM	2360	OH2	HOH	2023	-0.237	14.065	31.967	1.00	11.60		
ANISOU	2360	OH2	HOH	2023	1335	1136	1938	14	-417	104	
ATOM	2361	OH2	HOH	2024	19.982	14.750	19.390	1.00	11.75		
ANISOU	2361	OH2	HOH	2024	1473	1554	1438	-32	103	28	
ATOM	2362	OH2	HOH	2025	13.228	-5.984	23.216	1.00	12.24		
ANISOU	2362	OH2	HOH	2025	1443	1475	1733	-90	45	214	
ATOM	2363	OH2	HOH	2026	19.764	12.110	23.162	1.00	11.30		
ANISOU	2363	OH2	HOH	2026	1385	1165	1745	136	-1	6	
ATOM	2364	OH2	HOH	2027	21.917	10.821	46.070	1.00	12.10		
ANISOU	2364	OH2	HOH	2027	1706	1284	1606	-253	70	41	
ATOM	2365	OH2	HOH	2028	18.224	32.221	34.277	1.00	23.49		
ANISOU	2365	OH2	HOH	2028	3265	2841	2820	-537	-65	-455	
ATOM	2366	OH2	HOH	2029	9.399	32.606	33.563	1.00	14.45		
ANISOU	2366	OH2	HOH	2029	2294	1395	1801	239	35	-127	
ATOM	2367	OH2	HOH	2030	10.115	7.865	28.900	1.00	10.40		
ANISOU	2367	OH2	HOH	2030	1274	957	1719	-31	-116	106	
ATOM	2368	OH2	HOH	2031	11.030	33.108	36.020	1.00	14.06		
ANISOU	2368	OH2	HOH	2031	2205	1402	1734	137	81	34	

Table 1 (continued)

ATOM	2369	OH2	HOH	2032	30.731	24.856	38.865	1.00	12.21		
ANISOU	2369	OH2	HOH	2032	1090	1814	1734	139	90	-184	
ATOM	2370	OH2	HOH	2033	11.845	9.197	30.391	1.00	9.58		
ANISOU	2370	OH2	HOH	2033	1154	975	1510	175	-170	-64	
ATOM	2371	OH2	HOH	2034	24.995	32.489	45.432	1.00	11.85		
ANISOU	2371	OH2	HOH	2034	1049	1477	1975	100	-143	-163	
ATOM	2372	OH2	HOH	2035	13.731	17.090	17.376	1.00	12.56		
ANISOU	2372	OH2	HOH	2035	1706	1581	1484	23	127	-93	
ATOM	2373	OH2	HOH	2036	32.798	17.609	31.395	1.00	11.47		
ANISOU	2373	OH2	HOH	2036	1144	1657	1556	195	-179	158	
ATOM	2374	OH2	HOH	2037	13.336	8.586	22.450	1.00	11.15		
ANISOU	2374	OH2	HOH	2037	1388	1353	1496	-147	-53	-94	
ATOM	2375	OH2	HOH	2038	7.261	40.042	27.357	1.00	14.02		
ANISOU	2375	OH2	HOH	2038	1877	1236	2213	161	-78	-176	
ATOM	2376	OH2	HOH	2039	8.901	18.136	17.859	1.00	14.04		
ANISOU	2376	OH2	HOH	2039	1783	1508	2043	-97	-293	219	
ATOM	2377	OH2	HOH	2040	22.901	34.139	18.135	1.00	16.20		
ANISOU	2377	OH2	HOH	2040	2231	1532	2391	-244	16	-168	
ATOM	2378	OH2	HOH	2041	23.996	7.240	27.986	1.00	15.72		
ANISOU	2378	OH2	HOH	2041	1400	1337	3235	14	-27	18	
ATOM	2379	OH2	HOH	2042	24.993	23.182	18.913	1.00	16.24		
ANISOU	2379	OH2	HOH	2042	1807	2061	2302	435	320	101	
ATOM	2380	OH2	HOH	2043	19.148	5.661	41.077	1.00	12.85		
ANISOU	2380	OH2	HOH	2043	1775	1227	1881	93	80	301	
ATOM	2381	OH2	HOH	2044	24.501	28.878	32.387	1.00	20.46		
ANISOU	2381	OH2	HOH	2044	2385	2138	3249	-544	79	-601	
ATOM	2382	OH2	HOH	2045	11.870	34.623	33.554	1.00	22.76		
ANISOU	2382	OH2	HOH	2045	3018	2580	3049	909	-557	-1190	
ATOM	2383	OH2	HOH	2046	22.963	30.152	47.980	1.00	10.41		
ANISOU	2383	OH2	HOH	2046	1456	1125	1373	-149	-122	-146	
ATOM	2384	OH2	HOH	2047	-2.686	19.073	27.374	1.00	10.53		
ANISOU	2384	OH2	HOH	2047	912	1254	1836	26	-145	170	
ATOM	2385	OH2	HOH	2048	17.228	5.916	21.915	1.00	20.47		
ANISOU	2385	OH2	HOH	2048	2683	2370	2723	611	-208	-179	
ATOM	2386	OH2	HOH	2049	20.966	5.515	22.787	1.00	21.11		
ANISOU	2386	OH2	HOH	2049	3543	2077	2402	458	411	-168	
ATOM	2387	OH2	HOH	2050	18.808	35.973	20.701	1.00	22.96		
ANISOU	2387	OH2	HOH	2050	3279	2099	3346	296	-370	-120	
ATOM	2388	OH2	HOH	2051	22.527	22.497	16.149	1.00	15.06		
ANISOU	2388	OH2	HOH	2051	2078	1689	1956	52	53	-315	
ATOM	2389	OH2	HOH	2052	14.374	6.193	21.643	1.00	18.60		
ANISOU	2389	OH2	HOH	2052	2776	1935	2354	506	-354	-250	
ATOM	2390	OH2	HOH	2053	30.488	22.065	25.530	1.00	13.36		
ANISOU	2390	OH2	HOH	2053	1442	1894	1740	-203	-165	-112	
ATOM	2391	OH2	HOH	2054	24.217	9.898	21.086	1.00	23.35		
ANISOU	2391	OH2	HOH	2054	2905	2599	3367	906	63	-739	
ATOM	2392	OH2	HOH	2055	12.732	24.770	16.261	1.00	13.36		
ANISOU	2392	OH2	HOH	2055	2036	1650	1389	-178	168	-96	
ATOM	2393	OH2	HOH	2056	35.310	14.193	33.653	1.00	20.60		
ANISOU	2393	OH2	HOH	2056	1762	3205	2860	356	323	51	
ATOM	2394	OH2	HOH	2057	15.057	-2.873	25.824	1.00	18.01		

Table 1 (continued)

ANISOU	2394	OH2	HOH	2057	2788	1255	2800	-144	-775	116	
ATOM	2395	OH2	HOH	2058	3.861	28.991	35.199	1.00	18.52		
ANISOU	2395	OH2	HOH	2058	1763	2855	2420	213	-198	961	
ATOM	2396	OH2	HOH	2059	27.541	9.738	35.095	1.00	17.78		
ANISOU	2396	OH2	HOH	2059	1891	2061	2803	-223	395	-245	
ATOM	2397	OH2	HOH	2060	25.756	16.444	46.007	1.00	17.91		
ANISOU	2397	OH2	HOH	2060	1771	2586	2448	-428	-487	216	
ATOM	2398	OH2	HOH	2061	21.108	17.307	19.017	1.00	14.94		
ANISOU	2398	OH2	HOH	2061	2179	1477	2019	-266	357	-88	
ATOM	2399	OH2	HOH	2062	7.279	35.459	18.975	1.00	22.51		
ANISOU	2399	OH2	HOH	2062	2439	2916	3197	792	-55	270	
ATOM	2400	OH2	HOH	2063	22.491	30.103	32.617	1.00	21.37		
ANISOU	2400	OH2	HOH	2063	2255	2976	2889	-603	-705	842	
ATOM	2401	OH2	HOH	2064	22.615	10.885	18.887	1.00	19.80		
ANISOU	2401	OH2	HOH	2064	2809	1934	2782	42	175	-707	
ATOM	2402	OH2	HOH	2065	2.269	8.129	35.106	1.00	15.91		
ANISOU	2402	OH2	HOH	2065	2287	1527	2232	-220	-92	182	
ATOM	2403	OH2	HOH	2066	9.106	-3.515	39.745	1.00	26.06		
ANISOU	2403	OH2	HOH	2066	3641	2309	3951	179	-1365	458	
ATOM	2404	OH2	HOH	2067	20.845	22.193	14.148	1.00	18.98		
ANISOU	2404	OH2	HOH	2067	2479	2361	2372	61	-17	638	
ATOM	2405	OH2	HOH	2068	13.543	6.071	19.029	1.00	23.30		
ANISOU	2405	OH2	HOH	2068	3621	2014	3217	-352	-687	605	
ATOM	2406	OH2	HOH	2069	18.565	18.981	12.787	1.00	16.91		
ANISOU	2406	OH2	HOH	2069	2710	1821	1892	123	-26	46	
ATOM	2407	OH2	HOH	2070	18.359	21.142	14.600	1.00	14.84		
ANISOU	2407	OH2	HOH	2070	2166	1592	1880	195	-73	-17	
ATOM	2408	OH2	HOH	2071	4.366	11.191	46.702	1.00	23.90		
ANISOU	2408	OH2	HOH	2071	3983	2817	2280	180	-258	479	
ATOM	2409	OH2	HOH	2072	4.072	12.730	17.146	1.00	24.94		
ANISOU	2409	OH2	HOH	2072	3301	3045	3129	319	-435	-888	
ATOM	2410	OH2	HOH	2073	35.859	26.345	23.371	1.00	17.56		
ANISOU	2410	OH2	HOH	2073	1939	1917	2817	-48	90	351	
ATOM	2411	OH2	HOH	2074	18.868	6.807	23.957	1.00	19.27		
ANISOU	2411	OH2	HOH	2074	2094	2895	2334	-383	-23	-44	
ATOM	2412	OH2	HOH	2075	9.091	-0.413	41.963	1.00	26.22		
ANISOU	2412	OH2	HOH	2075	4785	2662	2516	921	0	578	
ATOM	2413	OH2	HOH	2076	16.112	2.843	21.594	1.00	19.95		
ANISOU	2413	OH2	HOH	2076	2733	2212	2635	-4	-260	92	
ATOM	2414	OH2	HOH	2077	18.485	19.782	17.034	1.00	17.00		
ANISOU	2414	OH2	HOH	2077	2420	2195	1846	24	53	-391	
ATOM	2415	OH2	HOH	2078	29.025	27.077	29.091	1.00	22.18		
ANISOU	2415	OH2	HOH	2078	2253	3097	3077	598	184	-244	
ATOM	2416	OH2	HOH	2079	19.760	17.529	16.504	1.00	27.43		
ANISOU	2416	OH2	HOH	2079	4340	3159	2922	-636	-664	-332	
ATOM	2417	OH2	HOH	2080	8.540	23.883	11.386	1.00	21.02		
ANISOU	2417	OH2	HOH	2080	3034	2540	2414	95	-812	-497	
ATOM	2418	OH2	HOH	2081	32.474	22.826	37.215	1.00	19.51		
ANISOU	2418	OH2	HOH	2081	1798	3082	2531	67	-761	339	
ATOM	2419	OH2	HOH	2082	21.545	11.232	16.522	1.00	26.38		
ANISOU	2419	OH2	HOH	2082	2902	3909	3212	1513	713	392	

Table 1 (continued)

ATOM	2420	OH2	HOH	2083	16.861	32.912	39.027	1.00	24.27		
ANISOU	2420	OH2	HOH	2083	4041	2361	2817	-597	-538	-127	
ATOM	2421	OH2	HOH	2084	9.457	26.048	46.967	1.00	32.61		
ANISOU	2421	OH2	HOH	2084	3972	3859	4559	-335	-739	-194	
ATOM	2422	OH2	HOH	2085	25.255	22.321	16.382	1.00	22.54		
ANISOU	2422	OH2	HOH	2085	2578	3324	2662	797	118	225	
ATOM	2423	OH2	HOH	2086	7.805	33.123	21.031	1.00	22.21		
ANISOU	2423	OH2	HOH	2086	2474	2898	3067	-89	-7	180	
ATOM	2424	OH2	HOH	2087	2.963	21.630	21.012	1.00	24.81		
ANISOU	2424	OH2	HOH	2087	3246	3288	2892	422	216	-522	
ATOM	2425	OH2	HOH	2088	12.611	-2.156	30.006	1.00	29.02		
ANISOU	2425	OH2	HOH	2088	5002	2469	3555	1133	57	319	
ATOM	2426	OH2	HOH	2089	28.315	11.728	30.582	1.00	18.77		
ANISOU	2426	OH2	HOH	2089	2184	1833	3113	424	-72	-218	
ATOM	2427	OH2	HOH	2090	0.495	6.125	34.745	1.00	25.84		
ANISOU	2427	OH2	HOH	2090	3436	2158	4223	-962	713	-537	
ATOM	2428	OH2	HOH	2091	16.120	19.247	45.953	1.00	25.44		
ANISOU	2428	OH2	HOH	2091	3973	2819	2875	97	574	-277	
ATOM	2429	OH2	HOH	2092	16.726	33.514	31.779	1.00	34.52		
ANISOU	2429	OH2	HOH	2092	4540	5165	3411	-2623	-686	-581	
ATOM	2430	OH2	HOH	2093	28.925	18.611	19.416	1.00	24.08		
ANISOU	2430	OH2	HOH	2093	2841	3620	2690	596	470	-189	
ATOM	2431	OH2	HOH	2094	29.000	18.421	40.799	1.00	30.10		
ANISOU	2431	OH2	HOH	2094	3522	3032	4881	229	-35	-348	
ATOM	2432	OH2	HOH	2095	25.850	11.412	45.963	1.00	19.48		
ANISOU	2432	OH2	HOH	2095	1907	2086	3408	256	14	909	
ATOM	2433	OH2	HOH	2096	20.009	37.070	24.551	1.00	27.14		
ANISOU	2433	OH2	HOH	2096	3277	3716	3319	-9	-693	-30	
ATOM	2434	OH2	HOH	2097	-0.741	10.653	36.389	1.00	27.10		
ANISOU	2434	OH2	HOH	2097	3762	2750	3783	-1375	-1082	1059	
ATOM	2435	OH2	HOH	2098	25.778	6.183	26.326	1.00	29.21		
ANISOU	2435	OH2	HOH	2098	2836	3824	4439	1152	1061	1265	
ATOM	2436	OH2	HOH	2099	20.635	33.299	-1.826	1.00	30.80		
ANISOU	2436	OH2	HOH	2099	5217	3154	3332	-1098	232	-415	
ATOM	2437	OH2	HOH	2100	23.679	15.862	19.292	1.00	27.46		
ANISOU	2437	OH2	HOH	2100	3779	3378	3278	503	53	28	
ATOM	2438	OH2	HOH	2101	28.642	11.615	33.283	1.00	18.91		
ANISOU	2438	OH2	HOH	2101	2364	1844	2978	194	182	160	
ATOM	2439	OH2	HOH	2102	20.500	30.664	34.595	1.00	29.66		
ANISOU	2439	OH2	HOH	2102	4477	3948	2846	1402	-136	-172	
ATOM	2440	OH2	HOH	2103	19.636	36.217	18.159	1.00	39.53		
ANISOU	2440	OH2	HOH	2103	5302	3739	5977	1897	-584	-61	
ATOM	2441	OH2	HOH	2104	22.561	35.055	28.392	1.00	27.57		
ANISOU	2441	OH2	HOH	2104	2551	3571	4355	-502	-407	-353	
ATOM	2442	OH2	HOH	2105	9.812	3.300	14.696	1.00	22.81		
ANISOU	2442	OH2	HOH	2105	2783	2692	3193	393	-704	-630	
ATOM	2443	OH2	HOH	2106	17.478	13.427	11.743	1.00	24.02		
ANISOU	2443	OH2	HOH	2106	3894	2847	2384	-506	379	34	
ATOM	2444	OH2	HOH	2107	18.319	21.596	1.717	1.00	37.21		
ANISOU	2444	OH2	HOH	2107	5869	3987	4284	-959	1727	-1356	
ATOM	2445	OH2	HOH	2108	0.147	-1.608	12.880	1.00	27.29		

Table 1 (continued)

ANISOU	2445	OH2	HOH	2108	2843	3741	3783	326	-894	-1356	
ATOM	2446	OH2	HOH	2109	6.268	18.645	18.883	1.00	22.59		
ANISOU	2446	OH2	HOH	2109	2918	2710	2956	139	-216	-411	
ATOM	2447	OH2	HOH	2110	16.838	-0.215	37.746	1.00	30.69		
ANISOU	2447	OH2	HOH	2110	4095	2373	5193	-296	-1720	189	
ATOM	2448	OH2	HOH	2111	25.258	32.534	41.448	1.00	27.41		
ANISOU	2448	OH2	HOH	2111	3973	1987	4456	-218	482	-926	
ATOM	2449	OH2	HOH	2112	2.223	25.051	13.896	1.00	28.20		
ANISOU	2449	OH2	HOH	2112	3984	2395	4337	6	-1010	-511	
ATOM	2450	OH2	HOH	2113	29.267	33.574	21.744	1.00	28.16		
ANISOU	2450	OH2	HOH	2113	2151	3744	4804	-674	328	-569	
ATOM	2451	OH2	HOH	2114	14.154	32.384	41.536	1.00	30.79		
ANISOU	2451	OH2	HOH	2114	2509	3569	5622	177	209	-1106	
ATOM	2452	OH2	HOH	2115	25.575	23.548	4.950	1.00	27.26		
ANISOU	2452	OH2	HOH	2115	3885	3085	3387	1053	-102	-289	
ATOM	2453	OH2	HOH	2116	21.593	7.334	20.867	1.00	27.89		
ANISOU	2453	OH2	HOH	2116	3321	3848	3429	535	-417	629	
ATOM	2454	OH2	HOH	2117	23.155	15.322	49.852	1.00	29.43		
ANISOU	2454	OH2	HOH	2117	5667	2625	2888	-741	-1410	-77	
ATOM	2455	OH2	HOH	2118	31.241	11.512	34.024	1.00	29.65		
ANISOU	2455	OH2	HOH	2118	1759	4478	5029	-73	391	1925	
ATOM	2456	OH2	HOH	2119	12.506	13.347	44.954	1.00	30.47		
ANISOU	2456	OH2	HOH	2119	4074	3073	4432	-416	225	29	
ATOM	2457	OH2	HOH	2120	9.137	42.977	4.644	1.00	28.80		
ANISOU	2457	OH2	HOH	2120	4403	3030	3511	268	177	-492	
ATOM	2458	OH2	HOH	2121	10.371	-4.559	22.096	1.00	25.99		
ANISOU	2458	OH2	HOH	2121	3180	2749	3946	847	777	439	
ATOM	2459	OH2	HOH	2122	-1.884	31.287	33.910	1.00	30.32		
ANISOU	2459	OH2	HOH	2122	4437	3474	3610	764	121	-284	
ATOM	2460	OH2	HOH	2123	11.926	2.902	16.437	1.00	34.58		
ANISOU	2460	OH2	HOH	2123	3807	4138	5194	1233	-1452	-828	
ATOM	2461	OH2	HOH	2124	31.395	25.003	42.826	1.00	31.68		
ANISOU	2461	OH2	HOH	2124	2510	3482	6045	484	-845	81	
ATOM	2462	OH2	HOH	2125	27.526	15.878	19.127	1.00	30.88		
ANISOU	2462	OH2	HOH	2125	4449	3902	3383	-518	-899	658	
ATOM	2463	OH2	HOH	2126	15.367	-0.963	15.516	1.00	49.85		
ANISOU	2463	OH2	HOH	2126	7256	5575	6111	1754	-27	279	
ATOM	2464	OH2	HOH	2127	26.630	29.902	34.801	1.00	29.70		
ANISOU	2464	OH2	HOH	2127	3399	3101	4786	-566	1487	-1057	
ATOM	2465	OH2	HOH	2128	5.907	37.376	1.732	1.00	28.32		
ANISOU	2465	OH2	HOH	2128	4487	3014	3260	-536	-1083	189	
ATOM	2466	OH2	HOH	2129	34.255	23.638	18.132	1.00	50.15		
ANISOU	2466	OH2	HOH	2129	6135	7075	5844	-476	1990	903	
ATOM	2467	OH2	HOH	2130	3.318	37.511	27.388	1.00	27.03		
ANISOU	2467	OH2	HOH	2130	2658	2481	5132	212	-550	-88	
ATOM	2468	OH2	HOH	2131	1.117	29.406	35.726	1.00	30.64		
ANISOU	2468	OH2	HOH	2131	3294	5110	3240	610	20	383	
ATOM	2469	OH2	HOH	2132	4.604	0.464	18.877	1.00	25.82		
ANISOU	2469	OH2	HOH	2132	3577	2371	3862	-157	-950	-139	
ATOM	2470	OH2	HOH	2133	-0.956	12.842	21.057	1.00	24.47		
ANISOU	2470	OH2	HOH	2133	3717	3027	2553	385	-684	-236	

Table 1 (continued)

ATOM	2471	OH2	HOH	2134	27.604	15.988	43.950	1.00	45.25		
ANISOU	2471	OH2	HOH	2134	3755	7222	6216	690	-1387	93	
ATOM	2472	OH2	HOH	2135	10.025	0.613	18.185	1.00	42.41		
ANISOU	2472	OH2	HOH	2135	6266	5193	4653	364	-513	-694	
ATOM	2473	OH2	HOH	2136	35.927	17.351	37.100	1.00	28.89		
ANISOU	2473	OH2	HOH	2136	2217	3925	4833	-556	-220	1242	
ATOM	2474	OH2	HOH	2137	5.594	19.454	44.164	1.00	42.26		
ANISOU	2474	OH2	HOH	2137	6586	5675	3798	-73	524	-39	
ATOM	2475	OH2	HOH	2138	23.132	22.600	45.476	1.00	25.88		
ANISOU	2475	OH2	HOH	2138	2245	4904	2686	346	-439	502	
ATOM	2476	OH2	HOH	2139	20.172	31.979	41.563	1.00	32.59		
ANISOU	2476	OH2	HOH	2139	2979	5289	4112	-345	255	-15	
ATOM	2477	OH2	HOH	2140	12.615	-3.457	32.659	1.00	29.56		
ANISOU	2477	OH2	HOH	2140	4077	3396	3758	197	444	282	
ATOM	2478	OH2	HOH	2141	29.893	13.167	28.439	1.00	36.82		
ANISOU	2478	OH2	HOH	2141	5526	3816	4649	-1141	34	-237	
ATOM	2479	OH2	HOH	2142	12.410	49.301	5.202	1.00	36.70		
ANISOU	2479	OH2	HOH	2142	5403	4305	4238	835	1728	-452	
ATOM	2480	OH2	HOH	2143	30.715	29.052	35.394	1.00	28.01		
ANISOU	2480	OH2	HOH	2143	3128	2641	4875	-241	-616	-997	
ATOM	2481	OH2	HOH	2144	17.281	34.142	-1.271	1.00	45.94		
ANISOU	2481	OH2	HOH	2144	7491	5662	4300	795	-289	1299	
ATOM	2482	OH2	HOH	2145	4.922	22.797	42.581	1.00	19.12		
ANISOU	2482	OH2	HOH	2145	3396	2327	1540	-411	509	-198	
ATOM	2483	OH2	HOH	2146	26.957	30.159	14.287	1.00	25.77		
ANISOU	2483	OH2	HOH	2146	3055	3169	3566	265	831	406	
ATOM	2484	OH2	HOH	2147	12.422	45.401	5.036	1.00	34.03		
ANISOU	2484	OH2	HOH	2147	3642	4631	4658	-181	355	-359	
ATOM	2485	OH2	HOH	2148	33.437	14.116	23.484	1.00	31.47		
ANISOU	2485	OH2	HOH	2148	3522	3389	5047	1058	397	882	
ATOM	2486	OH2	HOH	2149	0.164	4.431	23.666	1.00	33.84		
ANISOU	2486	OH2	HOH	2149	4637	4815	3406	154	538	-430	
ATOM	2487	OH2	HOH	2150	-1.460	28.447	34.307	1.00	28.09		
ANISOU	2487	OH2	HOH	2150	2705	3868	4101	337	152	-315	
ATOM	2488	OH2	HOH	2151	13.771	22.521	3.113	1.00	30.67		
ANISOU	2488	OH2	HOH	2151	5208	3547	2897	-542	-72	-845	
ATOM	2489	OH2	HOH	2152	28.782	29.818	29.002	1.00	47.73		
ANISOU	2489	OH2	HOH	2152	7348	5977	4811	1228	-875	839	
ATOM	2490	OH2	HOH	2153	7.137	15.243	42.731	1.00	29.71		
ANISOU	2490	OH2	HOH	2153	2540	4556	4193	805	148	7	
ATOM	2491	OH2	HOH	2154	23.785	46.053	8.991	1.00	38.34		
ANISOU	2491	OH2	HOH	2154	5125	4044	5399	-812	-1016	1182	
ATOM	2492	OH2	HOH	2155	33.133	20.243	38.315	1.00	36.79		
ANISOU	2492	OH2	HOH	2155	3714	5505	4760	1076	-517	-93	
ATOM	2493	OH2	HOH	2156	-0.820	9.533	18.799	1.00	41.36		
ANISOU	2493	OH2	HOH	2156	4360	5474	5882	1636	646	-129	
ATOM	2494	OH2	HOH	2157	18.652	5.079	19.622	1.00	29.73		
ANISOU	2494	OH2	HOH	2157	4286	3504	3508	264	-349	733	
ATOM	2495	OH2	HOH	2158	26.166	9.163	40.855	1.00	35.89		
ANISOU	2495	OH2	HOH	2158	3784	5241	4612	1346	-144	852	
ATOM	2496	OH2	HOH	2159	14.006	34.402	20.605	1.00	21.45		

Table 1 (continued)

ANISOU	2496	OH2	HOH	2159	2941	3370	1838	-794	136	154	
ATOM	2497	OH2	HOH	2160	34.840	11.129	34.976	1.00	38.19		
ANISOU	2497	OH2	HOH	2160	3440	6588	4481	697	-15	-1011	
ATOM	2498	OH2	HOH	2161	-1.988	5.242	23.285	1.00	62.11		
ANISOU	2498	OH2	HOH	2161	8575	7078	7945	192	1205	-866	
ATOM	2499	OH2	HOH	2162	25.277	29.730	9.669	1.00	38.83		
ANISOU	2499	OH2	HOH	2162	3194	5683	5876	-287	931	1477	
ATOM	2500	OH2	HOH	2163	13.817	35.649	32.918	1.00	37.06		
ANISOU	2500	OH2	HOH	2163	5619	3812	4648	1131	-941	1186	
ATOM	2501	OH2	HOH	2164	9.801	-1.515	21.959	1.00	32.73		
ANISOU	2501	OH2	HOH	2164	5130	3019	4287	622	-481	422	
ATOM	2502	OH2	HOH	2165	22.948	13.966	16.940	1.00	38.75		
ANISOU	2502	OH2	HOH	2165	5598	4725	4399	-470	118	-495	
ATOM	2503	OH2	HOH	2166	24.599	43.712	23.170	1.00	41.80		
ANISOU	2503	OH2	HOH	2166	4078	5118	6684	378	1519	-1220	
ATOM	2504	OH2	HOH	2167	14.615	17.699	47.486	1.00	39.85		
ANISOU	2504	OH2	HOH	2167	6879	4803	3458	1994	259	-707	
ATOM	2505	OH2	HOH	2168	1.445	21.717	40.470	1.00	33.88		
ANISOU	2505	OH2	HOH	2168	3815	5217	3841	-697	181	-1633	
ATOM	2506	OH2	HOH	2169	22.327	-3.798	28.767	1.00	40.30		
ANISOU	2506	OH2	HOH	2169	5793	4158	5361	-118	-1624	-544	
ATOM	2507	OH2	HOH	2170	-3.301	31.835	29.570	1.00	47.68		
ANISOU	2507	OH2	HOH	2170	4363	6351	7402	-268	1457	665	
ATOM	2508	OH2	HOH	2171	14.099	20.235	49.732	1.00	45.20		
ANISOU	2508	OH2	HOH	2171	5780	6657	4736	223	-383	-76	
ATOM	2509	OH2	HOH	2172	33.010	29.916	24.185	1.00	36.73		
ANISOU	2509	OH2	HOH	2172	3842	4642	5470	935	604	883	
ATOM	2510	OH2	HOH	2173	24.540	35.853	16.921	1.00	35.14		
ANISOU	2510	OH2	HOH	2173	5493	4104	3754	-2065	-882	1281	
ATOM	2511	OH2	HOH	2174	22.267	39.521	13.562	1.00	38.26		
ANISOU	2511	OH2	HOH	2174	4832	5278	4427	-154	-1914	-2304	
ATOM	2512	OH2	HOH	2175	27.448	18.787	44.469	1.00	37.82		
ANISOU	2512	OH2	HOH	2175	3810	4082	6476	300	-1875	1593	
ATOM	2513	OH2	HOH	2176	-5.528	7.324	24.580	1.00	39.48		
ANISOU	2513	OH2	HOH	2176	4104	5255	5641	-850	-256	33	
ATOM	2514	OH2	HOH	2177	-1.271	21.631	37.322	1.00	51.77		
ANISOU	2514	OH2	HOH	2177	6114	6078	7476	95	-1345	-992	
ATOM	2515	OH2	HOH	2178	31.545	33.928	23.456	1.00	35.45		
ANISOU	2515	OH2	HOH	2178	2867	4757	5847	-1426	392	-613	
ATOM	2516	OH2	HOH	2179	26.809	27.791	10.386	1.00	50.04		
ANISOU	2516	OH2	HOH	2179	8073	6525	4414	92	-1481	1021	
ATOM	2517	OH2	HOH	2180	16.434	43.287	-1.513	1.00	32.80		
ANISOU	2517	OH2	HOH	2180	5076	4302	3084	-1009	378	-806	
ATOM	2518	OH2	HOH	2181	0.515	1.244	23.642	1.00	46.07		
ANISOU	2518	OH2	HOH	2181	6632	5108	5766	-333	-625	-365	
ATOM	2519	OH2	HOH	2182	4.462	40.555	23.430	1.00	46.89		
ANISOU	2519	OH2	HOH	2182	5898	4762	7156	1683	168	-724	
ATOM	2520	OH2	HOH	2183	7.693	18.637	44.649	1.00	54.29		
ANISOU	2520	OH2	HOH	2183	5720	8062	6844	444	356	1599	
ATOM	2521	OH2	HOH	2184	16.308	3.941	19.161	1.00	41.90		
ANISOU	2521	OH2	HOH	2184	5275	5467	5177	722	1155	423	

Table 1 (continued)

ATOM	2522	OH2	HOH	2185	24.284	31.246	30.071	1.00	38.99		
ANISOU	2522	OH2	HOH	2185	3156	6579	5081	-671	1673	405	
ATOM	2523	OH2	HOH	2186	3.278	26.568	41.478	1.00	38.84		
ANISOU	2523	OH2	HOH	2186	4518	5116	5126	-518	2217	-1485	
ATOM	2524	OH2	HOH	2187	3.639	19.957	19.606	1.00	40.15		
ANISOU	2524	OH2	HOH	2187	4585	5844	4825	-498	-1941	1112	
ATOM	2525	OH2	HOH	2188	21.631	33.310	34.590	1.00	63.14		
ANISOU	2525	OH2	HOH	2188	8075	8637	7279	-728	183	-1126	
ATOM	2526	OH2	HOH	2189	32.720	29.399	21.712	1.00	53.84		
ANISOU	2526	OH2	HOH	2189	4431	7584	8441	52	-467	-206	
ATOM	2527	OH2	HOH	2190	24.376	3.189	30.591	1.00	50.03		
ANISOU	2527	OH2	HOH	2190	6412	6632	5966	275	-2344	589	
ATOM	2528	OH2	HOH	2191	-4.748	4.483	26.356	1.00	42.58		
ANISOU	2528	OH2	HOH	2191	4725	4619	6834	-557	-249	-1132	
ATOM	2529	OH2	HOH	2192	-6.926	8.039	28.059	1.00	43.47		
ANISOU	2529	OH2	HOH	2192	3521	5622	7375	418	180	553	
ATOM	2530	OH2	HOH	2193	14.237	53.526	3.775	1.00	55.14		
ANISOU	2530	OH2	HOH	2193	7223	7276	6451	657	606	-1397	
ATOM	2531	OH2	HOH	2194	9.458	12.921	44.597	1.00	36.74		
ANISOU	2531	OH2	HOH	2194	6936	4199	2826	-1801	1015	58	
ATOM	2532	OH2	HOH	2195	0.251	3.079	35.433	1.00	46.34		
ANISOU	2532	OH2	HOH	2195	5953	7035	4619	1756	-784	-592	
ATOM	2533	OH2	HOH	2196	25.829	31.812	1.275	1.00	61.39		
ANISOU	2533	OH2	HOH	2196	7957	7943	7426	-1266	689	-159	
ATOM	2534	OH2	HOH	2197	5.655	-1.834	39.466	1.00	52.65		
ANISOU	2534	OH2	HOH	2197	5708	7338	6960	672	-532	941	
ATOM	2535	OH2	HOH	2198	19.706	3.198	23.260	1.00	66.22		
ANISOU	2535	OH2	HOH	2198	7117	9716	8327	-157	1989	-532	
ATOM	2536	OH2	HOH	2199	15.408	14.624	11.007	1.00	55.81		
ANISOU	2536	OH2	HOH	2199	8534	5674	6999	1238	-109	-1873	
ATOM	2537	OH2	HOH	2200	3.804	11.778	14.191	1.00	35.90		
ANISOU	2537	OH2	HOH	2200	4584	3990	5068	-835	-1773	1552	
ATOM	2538	OH2	HOH	2201	10.699	20.908	50.371	1.00	48.49		
ANISOU	2538	OH2	HOH	2201	6598	7024	4801	-2364	-1174	534	
ATOM	2539	OH2	HOH	2202	26.392	3.610	27.263	1.00	40.02		
ANISOU	2539	OH2	HOH	2202	3983	4878	6343	1531	-1650	-566	
ATOM	2540	OH2	HOH	2203	24.061	34.160	31.029	1.00	64.19		
ANISOU	2540	OH2	HOH	2203	7352	8511	8525	-280	426	1171	
ATOM	2541	OH2	HOH	2204	2.116	45.934	9.846	1.00	44.68		
ANISOU	2541	OH2	HOH	2204	6736	4342	5899	-650	-622	-484	
ATOM	2542	OH2	HOH	2205	6.445	43.337	4.182	1.00	61.78		
ANISOU	2542	OH2	HOH	2205	8972	7223	7277	1088	-879	-922	
ATOM	2543	OH2	HOH	2206	10.542	43.839	0.866	1.00	41.73		
ANISOU	2543	OH2	HOH	2206	5634	5406	4817	-452	-745	-710	
ATOM	2544	OH2	HOH	2207	14.080	18.324	4.687	1.00	51.79		
ANISOU	2544	OH2	HOH	2207	7044	6269	6363	824	1136	-1751	
ATOM	2545	OH2	HOH	2208	15.234	47.925	10.270	1.00	46.92		
ANISOU	2545	OH2	HOH	2208	7004	6456	4368	-1808	1022	-870	
ATOM	2546	OH2	HOH	2209	16.967	45.194	9.967	1.00	47.86		
ANISOU	2546	OH2	HOH	2209	6299	5224	6664	-1081	1350	2059	
ATOM	2547	OH2	HOH	2210	15.117	44.426	8.848	1.00	49.55		

Table 1 (continued)

ANISOU	2547	OH2	HOH	2210	7681	6916	4228	537	429	2327	
ATOM	2548	OH2	HOH	2211	12.361	44.070	7.558	1.00	44.73		
ANISOU	2548	OH2	HOH	2211	5836	5538	5622	45	547	-1911	
ATOM	2549	OH2	HOH	2212	18.430	36.878	14.596	1.00	15.94		
ANISOU	2549	OH2	HOH	2212	2599	1411	2047	20	306	176	
ATOM	2550	OH2	HOH	2213	1.950	23.756	18.336	1.00	54.26		
ANISOU	2550	OH2	HOH	2213	7029	7331	6257	-368	1018	-1458	
ATOM	2551	OH2	HOH	2214	4.070	23.111	18.945	1.00	22.11		
ANISOU	2551	OH2	HOH	2214	4024	1919	2458	-603	-473	251	
ATOM	2552	OH2	HOH	2215	-4.930	30.563	15.734	1.00	47.61		
ANISOU	2552	OH2	HOH	2215	5138	6978	5972	-1286	1047	-490	
ATOM	2553	OH2	HOH	2216	3.493	39.603	19.806	1.00	79.97		
ANISOU	2553	OH2	HOH	2216	9936	10609	9839	1122	2485	-126	
ATOM	2554	OH2	HOH	2217	8.338	37.431	20.460	1.00	40.15		
ANISOU	2554	OH2	HOH	2217	5741	4899	4614	-770	-483	-246	
ATOM	2555	OH2	HOH	2218	14.473	35.604	35.443	1.00	60.51		
ANISOU	2555	OH2	HOH	2218	9411	6844	6735	1048	-373	-2889	
ATOM	2556	OH2	HOH	2219	21.237	38.091	20.801	1.00	53.48		
ANISOU	2556	OH2	HOH	2219	5494	7528	7298	-45	234	965	
ATOM	2557	OH2	HOH	2220	17.262	37.265	23.919	1.00	29.72		
ANISOU	2557	OH2	HOH	2220	2730	2018	6544	-555	-547	-486	
ATOM	2558	OH2	HOH	2221	31.875	27.365	22.361	1.00	38.97		
ANISOU	2558	OH2	HOH	2221	4117	5587	5101	76	284	2321	
ATOM	2559	OH2	HOH	2222	33.178	17.244	20.397	1.00	27.94		
ANISOU	2559	OH2	HOH	2222	2657	4414	3543	1272	-969	-1929	
ATOM	2560	OH2	HOH	2223	34.367	12.125	22.041	1.00	34.43		
ANISOU	2560	OH2	HOH	2223	4472	3185	5425	358	-1759	-77	
ATOM	2561	OH2	HOH	2224	0.095	32.901	35.929	1.00	57.21		
ANISOU	2561	OH2	HOH	2224	7358	7653	6727	-800	2273	-457	
ATOM	2562	OH2	HOH	2225	-1.851	34.924	31.401	1.00	60.17		
ANISOU	2562	OH2	HOH	2225	8741	6000	8122	1146	-1427	121	
ATOM	2563	OH2	HOH	2226	1.338	35.092	31.643	1.00	42.29		
ANISOU	2563	OH2	HOH	2226	7071	3923	5073	532	816	457	
ATOM	2564	OH2	HOH	2227	4.978	19.377	10.874	1.00	63.72		
ANISOU	2564	OH2	HOH	2227	8573	7361	8277	1912	-1119	1781	
ATOM	2565	OH2	HOH	2228	20.151	13.048	12.891	1.00	51.34		
ANISOU	2565	OH2	HOH	2228	7243	8866	3398	-155	176	-2115	
ATOM	2566	OH2	HOH	2229	3.446	6.655	10.378	1.00	43.66		
ANISOU	2566	OH2	HOH	2229	5444	4844	6301	183	-922	1114	
ATOM	2567	OH2	HOH	2230	-1.076	11.025	16.564	1.00	49.47		
ANISOU	2567	OH2	HOH	2230	6690	6163	5945	-4	453	-139	
ATOM	2568	OH2	HOH	2231	-2.344	12.956	18.471	1.00	51.91		
ANISOU	2568	OH2	HOH	2231	5617	6959	7149	-2077	-1139	-224	
ATOM	2569	OH2	HOH	2232	-3.012	10.591	30.199	1.00	23.98		
ANISOU	2569	OH2	HOH	2232	2569	2824	3716	-613	-569	-357	
ATOM	2570	OH2	HOH	2233	13.701	4.031	40.758	1.00	36.30		
ANISOU	2570	OH2	HOH	2233	4928	4518	4348	-2174	-1320	188	
ATOM	2571	OH2	HOH	2234	15.955	2.640	38.888	1.00	28.93		
ANISOU	2571	OH2	HOH	2234	2375	3941	4675	-115	-130	1875	
ATOM	2572	OH2	HOH	2235	20.816	5.954	33.830	1.00	22.40		
ANISOU	2572	OH2	HOH	2235	2205	3848	2460	1125	66	877	

Table 1 (continued)

ATOM	2573	OH2	HOH	2236	20.630	5.992	31.109	1.00	15.17		
ANISOU	2573	OH2	HOH	2236	1772	2101	1888	301	135	-133	
ATOM	2574	OH2	HOH	2237	27.186	13.272	42.527	1.00	49.68		
ANISOU	2574	OH2	HOH	2237	5444	6390	7043	143	903	1186	
ATOM	2575	OH2	HOH	2238	25.721	6.161	42.843	1.00	45.13		
ANISOU	2575	OH2	HOH	2238	5375	7059	4712	-478	1664	2478	
ATOM	2576	OH2	HOH	2239	3.314	19.807	43.160	1.00	43.78		
ANISOU	2576	OH2	HOH	2239	5811	6204	4619	251	129	-1537	
ATOM	2577	OH2	HOH	2240	4.297	27.027	37.081	1.00	17.90		
ANISOU	2577	OH2	HOH	2240	1612	1958	3230	5	-222	859	
ATOM	2578	OH2	HOH	2241	16.988	23.992	46.245	1.00	52.67		
ANISOU	2578	OH2	HOH	2241	7222	5800	6992	116	-530	-1014	
ATOM	2579	OH2	HOH	2242	-2.377	39.990	14.418	1.00	41.88		
ANISOU	2579	OH2	HOH	2242	4845	5991	5078	-1456	-193	-1024	
ATOM	2580	OH2	HOH	2243	3.130	42.450	7.749	1.00	42.10		
ANISOU	2580	OH2	HOH	2243	6306	4786	4904	1497	-47	-377	
ATOM	2581	OH2	HOH	2244	2.997	44.684	6.699	1.00	56.28		
ANISOU	2581	OH2	HOH	2244	6235	7348	7800	609	-1439	1125	
ATOM	2582	OH2	HOH	2245	22.890	45.174	0.987	1.00	48.36		
ANISOU	2582	OH2	HOH	2245	5179	6800	6398	-116	-592	49	
ATOM	2583	OH2	HOH	2246	15.568	38.121	17.923	1.00	30.65		
ANISOU	2583	OH2	HOH	2246	4597	3182	3868	-409	196	287	
ATOM	2584	OH2	HOH	2247	16.944	38.683	16.010	1.00	36.47		
ANISOU	2584	OH2	HOH	2247	4444	4968	4443	205	238	-1717	
ATOM	2585	OH2	HOH	2248	6.823	40.208	15.789	1.00	55.71		
ANISOU	2585	OH2	HOH	2248	6916	7528	6725	130	-803	312	
ATOM	2586	OH2	HOH	2249	10.350	40.659	13.664	1.00	42.28		
ANISOU	2586	OH2	HOH	2249	6130	4786	5150	530	-1597	354	
ATOM	2587	OH2	HOH	2250	22.047	15.825	15.658	1.00	46.32		
ANISOU	2587	OH2	HOH	2250	6365	6760	4473	-442	1535	-48	
ATOM	2588	OH2	HOH	2251	15.675	3.412	16.780	1.00	55.34		
ANISOU	2588	OH2	HOH	2251	7688	6918	6420	188	-1221	-87	
ATOM	2589	OH2	HOH	2252	14.677	5.481	14.790	1.00	45.59		
ANISOU	2589	OH2	HOH	2252	6170	4087	7064	112	-194	-788	
ATOM	2590	OH2	HOH	2253	6.512	4.458	37.967	1.00	16.65		
ANISOU	2590	OH2	HOH	2253	1744	1336	3246	-7	65	-45	
ATOM	2591	OH2	HOH	2254	27.055	21.820	46.605	1.00	50.56		
ANISOU	2591	OH2	HOH	2254	5419	7304	6488	-461	757	1307	
ATOM	2592	OH2	HOH	2255	34.498	18.342	18.221	1.00	54.53		
ANISOU	2592	OH2	HOH	2255	5989	6366	8364	-2444	-1601	-355	
ATOM	2593	OH2	HOH	2256	35.334	16.235	18.626	1.00	54.98		
ANISOU	2593	OH2	HOH	2256	5757	8014	7121	-515	-1092	228	
ATOM	2594	OH2	HOH	2257	31.131	14.648	22.506	1.00	36.00		
ANISOU	2594	OH2	HOH	2257	3978	3116	6586	-110	-1576	-1470	
ATOM	2595	OH2	HOH	2258	33.181	10.274	21.383	1.00	44.81		
ANISOU	2595	OH2	HOH	2258	5022	5790	6214	-1090	923	-1286	
ATOM	2596	OH2	HOH	2259	24.252	4.912	23.515	1.00	45.87		
ANISOU	2596	OH2	HOH	2259	7208	4670	5550	1464	1751	-896	
ATOM	2597	OH2	HOH	2260	1.663	22.210	43.867	1.00	70.15		
ANISOU	2597	OH2	HOH	2260	8197	8982	9474	68	337	-2	
ATOM	2598	OH2	HOH	2261	-0.515	19.931	40.430	1.00	39.90		

Table 1 (continued)

ANISOU	2598	OH2	HOH	2261	5209	3243	6710	813	217	505	
ATOM	2599	OH2	HOH	2262	-2.457	19.610	38.621	1.00	41.31		
ANISOU	2599	OH2	HOH	2262	4325	6734	4637	-249	-924	-1772	
ATOM	2600	OH2	HOH	2263	-0.166	21.593	35.310	1.00	28.83		
ANISOU	2600	OH2	HOH	2263	4611	2357	3987	429	-1182	-689	
ATOM	2601	OH2	HOH	2264	13.689	21.920	52.636	1.00	44.27		
ANISOU	2601	OH2	HOH	2264	4121	5106	7593	836	-564	213	
ATOM	2602	OH2	HOH	2265	19.920	1.651	29.589	1.00	21.53		
ANISOU	2602	OH2	HOH	2265	2354	2225	3601	-47	-357	-16	
ATOM	2603	OH2	HOH	2266	19.598	3.372	31.578	1.00	40.81		
ANISOU	2603	OH2	HOH	2266	5438	4607	5460	961	-1985	1076	
ATOM	2604	OH2	HOH	2267	22.242	1.810	32.147	1.00	92.82		
ANISOU	2604	OH2	HOH	2267	12020	11512	11735	546	661	-132	
ATOM	2605	OH2	HOH	2268	14.772	-2.224	28.848	1.00	24.79		
ANISOU	2605	OH2	HOH	2268	3712	2086	3622	54	-457	149	
ATOM	2606	OH2	HOH	2269	17.749	-2.449	30.658	1.00	57.30		
ANISOU	2606	OH2	HOH	2269	8357	6705	6708	1697	-64	1200	
ATOM	2607	OH2	HOH	2270	10.519	39.894	17.375	1.00	62.82		
ANISOU	2607	OH2	HOH	2270	8324	6608	8938	1679	1813	-368	
ATOM	2608	OH2	HOH	2271	0.430	11.820	14.684	1.00	45.51		
ANISOU	2608	OH2	HOH	2271	6282	5127	5882	-400	-439	-2108	
ATOM	2609	OH2	HOH	2272	5.668	12.613	13.139	1.00	70.99		
ANISOU	2609	OH2	HOH	2272	8991	8796	9187	274	94	-923	
ATOM	2610	OH2	HOH	2273	-8.237	7.562	23.932	1.00	52.58		
ANISOU	2610	OH2	HOH	2273	7204	6080	6693	-1479	-2517	-908	
ATOM	2611	OH2	HOH	2274	-5.548	10.089	31.128	1.00	50.96		
ANISOU	2611	OH2	HOH	2274	7124	5031	7208	1698	-778	-200	
ATOM	2612	OH2	HOH	2275	6.006	3.285	39.881	1.00	59.05		
ANISOU	2612	OH2	HOH	2275	5232	9368	7837	-816	-907	-141	
ATOM	2613	OH2	HOH	2276	18.329	3.511	35.187	1.00	31.14		
ANISOU	2613	OH2	HOH	2276	3603	3616	4612	-55	174	-18	
ATOM	2614	OH2	HOH	2277	17.197	4.413	39.613	1.00	32.09		
ANISOU	2614	OH2	HOH	2277	3756	5397	3039	1046	-881	-147	
ATOM	2615	OH2	HOH	2278	18.186	1.261	41.660	1.00	41.10		
ANISOU	2615	OH2	HOH	2278	5188	4409	6021	-602	1680	-703	
ATOM	2616	OH2	HOH	2279	17.739	1.394	15.973	1.00	57.56		
ANISOU	2616	OH2	HOH	2279	7591	8946	5333	-164	1856	-1008	
ATOM	2617	OH2	HOH	2280	14.323	0.199	17.194	1.00	73.92		
ANISOU	2617	OH2	HOH	2280	9181	9903	9003	502	-21	-2853	
ATOM	2618	OH2	HOH	2281	8.551	41.455	14.905	1.00	118.27		
ANISOU	2618	OH2	HOH	2281	15164	14719	15054	-78	-125	-146	
ATOM	2619	OH2	HOH	2282	12.963	40.910	13.215	1.00	50.68		
ANISOU	2619	OH2	HOH	2282	5704	7547	6006	-155	1499	562	
ATOM	2620	OH2	HOH	2283	11.294	41.629	11.806	1.00	66.06		
ANISOU	2620	OH2	HOH	2283	7867	8521	8711	-456	228	379	
ATOM	2621	OH2	HOH	2284	16.077	39.615	-1.846	1.00	40.93		
ANISOU	2621	OH2	HOH	2284	6295	4439	4819	1068	-22	-778	
ATOM	2622	OH2	HOH	2285	26.136	25.331	7.947	1.00	44.29		
ANISOU	2622	OH2	HOH	2285	4768	6987	5074	212	-40	-211	
ATOM	2623	OH2	HOH	2286	21.800	18.302	10.818	1.00	62.90		
ANISOU	2623	OH2	HOH	2286	7374	8435	8089	-341	-1040	217	

Table 1 (continued)

ATOM	2624	OH2	HOH	2287	20.645	15.005	9.508	1.00	65.90		
ANISOU	2624	OH2	HOH	2287	7740	8042	9257	721	-271	672	
ATOM	2625	OH2	HOH	2288	18.387	3.421	15.099	1.00	49.21		
ANISOU	2625	OH2	HOH	2288	6380	6528	5791	-510	971	-48	
ATOM	2626	OH2	HOH	2289	24.587	9.772	18.510	1.00	57.54		
ANISOU	2626	OH2	HOH	2289	6543	7549	7769	-419	-226	1288	
ATOM	2627	OH2	HOH	2290	25.543	11.619	19.500	1.00	71.38		
ANISOU	2627	OH2	HOH	2290	8517	9042	9563	1529	-52	864	
ATOM	2628	OH2	HOH	2291	33.783	12.038	33.174	1.00	35.32		
ANISOU	2628	OH2	HOH	2291	3767	4658	4996	-371	1350	-758	
ATOM	2629	OH2	HOH	2292	-3.299	8.740	32.299	1.00	39.11		
ANISOU	2629	OH2	HOH	2292	3342	5678	5839	-303	342	-514	
ATOM	2630	OH2	HOH	2293	7.138	-6.198	35.152	1.00	36.60		
ANISOU	2630	OH2	HOH	2293	5059	3091	5757	-1009	1251	-1152	
ATOM	2631	OH2	HOH	2294	0.994	4.645	36.942	1.00	50.65		
ANISOU	2631	OH2	HOH	2294	6021	6739	6487	-816	1270	-1075	
ATOM	2632	OH2	HOH	2295	-0.106	6.688	39.157	1.00	49.06		
ANISOU	2632	OH2	HOH	2295	4516	7809	6315	-1468	564	-1932	
ATOM	2633	OH2	HOH	2296	21.634	37.338	18.355	1.00	50.95		
ANISOU	2633	OH2	HOH	2296	7051	5878	6429	-955	-1767	-1051	
ATOM	2634	OH2	HOH	2297	7.045	37.657	18.368	1.00	44.09		
ANISOU	2634	OH2	HOH	2297	4574	4722	7459	242	491	593	
ATOM	2635	OH2	HOH	2298	18.268	34.358	30.180	1.00	37.05		
ANISOU	2635	OH2	HOH	2298	4092	6214	3772	-749	165	411	
ATOM	2636	OH2	HOH	2299	7.692	41.068	10.258	1.00	51.21		
ANISOU	2636	OH2	HOH	2299	5855	8339	5263	441	1330	-2664	
ATOM	2637	OH2	HOH	2300	6.986	-7.646	33.375	1.00	32.81		
ANISOU	2637	OH2	HOH	2300	4060	3716	4691	1275	-2322	-704	
ATOM	2638	OH2	HOH	2301	-8.782	30.474	8.939	1.00	40.24		
ANISOU	2638	OH2	HOH	2301	4217	5588	5484	-1619	54	693	
ATOM	2639	OH2	HOH	2302	13.681	34.760	-0.596	1.00	52.86		
ANISOU	2639	OH2	HOH	2302	6814	7897	5372	-621	-1484	1274	
ATOM	2640	OH2	HOH	2303	23.230	42.983	0.375	1.00	49.35		
ANISOU	2640	OH2	HOH	2303	4517	8177	6057	139	575	1267	
ATOM	2641	OH2	HOH	2305	-7.452	29.742	10.799	1.00	46.13		
ANISOU	2641	OH2	HOH	2305	5250	5278	7000	2086	-1259	578	
ATOM	2642	OH2	HOH	2306	-6.412	30.758	28.400	1.00	53.77		
ANISOU	2642	OH2	HOH	2306	7895	4856	7680	1834	-2211	1056	
ATOM	2643	OH2	HOH	2307	24.528	7.914	33.885	1.00	52.07		
ANISOU	2643	OH2	HOH	2307	5908	6787	7090	3063	-2150	1040	
ATOM	2644	OH2	HOH	2308	3.162	37.461	31.203	1.00	42.70		
ANISOU	2644	OH2	HOH	2308	3898	5376	6950	553	123	-1855	
ATOM	2645	OH2	HOH	2309	27.344	34.345	6.979	1.00	53.05		
ANISOU	2645	OH2	HOH	2309	7198	6157	6803	524	2	1342	
ATOM	2646	OH2	HOH	2310	8.352	28.846	0.587	1.00	48.08		
ANISOU	2646	OH2	HOH	2310	7283	6918	4066	-1595	-1926	-1593	
ATOM	2647	OH2	HOH	2311	27.043	12.975	47.864	1.00	57.97		
ANISOU	2647	OH2	HOH	2311	7623	7911	6494	-2096	1729	2454	
ATOM	2648	OH2	HOH	2312	9.482	42.324	-1.614	1.00	44.75		
ANISOU	2648	OH2	HOH	2312	5120	4765	7117	308	1106	1780	
ATOM	2649	OH2	HOH	2313	-8.801	35.732	7.848	1.00	57.76		

Table 1 (continued)

ANISOU	2649	OH2	HOH	2313	5517	7910	8518	616	-382	-1402	
ATOM	2650	OH2	HOH	2314	-0.455	18.736	16.444	1.00	43.01		
ANISOU	2650	OH2	HOH	2314	5291	6758	4295	749	-1815	729	
ATOM	2651	OH2	HOH	2315	7.574	-1.992	20.640	1.00	46.37		
ANISOU	2651	OH2	HOH	2315	5569	5373	6675	-156	-41	1686	
ATOM	2652	OH2	HOH	2318	3.833	31.378	36.561	1.00	53.11		
ANISOU	2652	OH2	HOH	2318	6350	5805	8024	1840	-613	-1091	

[0127] The variations in coordinates discussed above may be generated because of mathematical manipulations of the HGFR-Compound **1** complex structure coordinates. For example, the structure coordinates set forth in Table 1 could be manipulated by crystallographic permutations of the structure coordinates, fractionalization of the structure coordinates, integer additions or subtractions to sets of the structure coordinates, or combinations thereof.

[0128] Alternatively, modifications in the crystal structure due to mutations, additions, substitutions, and/or deletions of amino acids, or other changes in any of the components that make up the crystal could also account for variations in structure coordinates. If such variations are within an acceptable standard error as compared to the original coordinates, the resulting three-dimensional shape is considered to be the same. Thus, for example, a ligand that bound to the binding pocket of the HGFR domain would also be expected to bind to another binding pocket whose structure coordinates when compared to those described have a root mean square difference of equal to or less than about 1.5 Å, more preferably less than about 1.0 Å, and even more preferably less than about 0.5 Å, from the backbone atoms.

[0129] Various computational analyses can be performed to determine whether a polypeptide or the binding pocket portion thereof is sufficiently similar to the HGFR binding pocket as described herein. Such analyses may be carried out through the use of known software applications, such as ProMod, SWISS-MODEL (Swiss Institute of Bioinformatics), and the Molecular Similarity application of QUANTA (Accelrys, Inc., San Diego, CA). Programs, such as QUANTA permit comparisons between different structures, different conformations of the same structure, and different parts of the same structure. Comparison of structures using such computer software may involve the following steps: 1) loading the structures to be compared; 2) defining the atom equivalencies in the structures; 3) performing a fitting operation; and 4) analyzing the results. Each structure is identified by a name. One structure is identified as the target (i.e., the fixed structure); all remaining structures are working structures (i.e., moving structures). Since atom equivalency with QUANTA is defined by user input, for the purpose of this invention applicants define equivalent atoms as protein backbone atoms (N, Cα, C, and O) for all conserved residues between the two structures being compared. We will also consider only rigid fitting operations. When a rigid fitting method is used, the working structure is translated and rotated to obtain an optimum fit with the target structure. The fitting operation uses an algorithm that computes the optimum translation and rotation to be applied to the moving structure, such that the root mean square difference of the fit over the specified pairs of equivalent atoms is an absolute minimum. This number, given in angstroms (Å), is reported by software applications, such as QUANTA.

[0130] For the purpose of this invention, any HGFR molecule or molecular complex or binding pocket thereof that has a root mean square deviation of conserved residue backbone atoms (N, Cα, C, O) of less than about 1.5 Å, more preferably less than about 1.0 Å, and even more preferably less than about 0.5 Å, when superimposed on the relevant backbone atoms described by structure coordinates listed in Table 1 are considered equivalent.

[0131] The term "root mean square deviation" means the square root of the arithmetic mean of the squares of the deviations from the mean. It is a way to express the deviation or variation from a trend or object. For purposes of this invention, the "root mean square deviation" defines the variation in the backbone of a protein from the backbone of the HGFR polypeptides of the invention or the HGFR substrate-binding domain portion thereof, as defined by the structure coordinates described herein.

E. Computers, Computer Software, Computer Modeling

[0132] One embodiment of the invention includes a computer for producing a three-dimensional representation of the HGFR domain of the polypeptides of the invention and complexes of the HGFR domain of such polypeptides with a ligand.

[0133] Computers are known in the art and may include a central processing unit (CPU), a working memory, which can be random-access memory, core memory, mass-storage memory, or combinations of all of the aforementioned. The CPU may encode one or more programs. Computers may also include display, and input and output devices, such as one or more cathode-ray tube display terminals, keyboards, modems, input lines and output lines. Persons skilled in the computer art will understand that many variations of a computer exist in the art and all such variations are

applicable to the present invention. Further, said computers may be networked to computer servers (the machine on which large calculations can be run in batch), and file servers (the main machine for all the centralized databases).

[0134] Machine-readable media containing data, such as the crystal structure coordinates of the polypeptides of the invention may be inputted using various hardware, including modems, CD-ROM drives, disk drives, or keyboards.

[0135] Output hardware, such as a CRT display terminal may be used for displaying a graphical representation of the HGFR polypeptide of the invention or the HGFR substrate-binding domain of these polypeptides using a program such as QUANTA. Output hardware may also include a printer, and disk drives.

[0136] The CPU coordinates the use of the various input and output devices, coordinates data accesses from storage and accesses to and from working memory, and determines the sequence of data processing steps. A number of programs may be used to process the machine-readable data of this invention. Such programs are discussed in reference to the computational methods of drug discovery as described herein.

[0137] Thus, one embodiment of the present invention includes X-ray coordinate data capable of being processed into a three dimensional graphical display of a molecule or molecular complex that comprises an HGFR-like substrate-binding pocket stored in a machine-readable storage medium. The three-dimensional structure of a molecule or molecular complex comprising an HGFR-like substrate-binding pocket may be used for a variety of purposes, such as drug discovery.

[0138] For example, the three- dimensional structure derived from the structure coordinate data may be computationally evaluated for its ability to associate with chemical entities. Such entities would be potential drug candidates and would be evaluated for their ability to inhibit or modulate the activity of HGFR.

[0139] The term "chemical entity," as used herein, refers to chemical compounds, complexes of at least two chemical compounds, and fragments of such compounds or complexes.

[0140] Throughout this section, discussions about the ability of an entity to bind to, or associate with an HGFR-like substrate-binding domain refer to features of the entity alone. Assays to determine if a compound binds to HGFR are known in the art and are exemplified herein.

[0141] The design of compounds that bind to HGFR-like substrate-binding domains according to this invention may involve consideration of two factors. First, the entity must be capable of physically and structurally associating with some or the entire HGFR-like substrate-binding domain. Non-covalent molecular interactions important in this association include hydrogen bonding, van der Waals interactions, hydrophobic interactions and electrostatic interactions.

[0142] The term "associating with" refers to a condition of proximity between a chemical entity or compound, or portions thereof, and a binding pocket or binding site on a protein. The association may be non-covalent, for example, wherein the juxtaposition is energetically favored by hydrogen bonding of van der Waals or electrostatic interactions, or it may be covalent.

[0143] Second, the entity must be able to assume a conformation that allows it to associate with the HGFR-like substrate-binding domain directly. Although certain portions of the entity will not directly participate in these associations, those portions of the entity may still influence the overall conformation of the molecule. This, in turn, may have a significant impact on potency. Such conformational requirements include the overall three-dimensional structure and orientation of the chemical entity in relation to all or a portion of the binding pocket, or the spacing between functional groups of an entity comprising several chemical entities that directly interact with the HGFR-like-binding pocket or homologues thereof.

[0144] The potential inhibitory or binding effect of a chemical entity on an HGFR-like substrate-binding domain may be analyzed prior to its actual synthesis and testing through the use of computer-modeling techniques. If the theoretical structure of the given entity suggests insufficient interaction and association between it and the HGFR-like-binding pocket, further testing of the entity may not be necessary. However, if computer modeling indicates a strong interaction, the molecule can be synthesized and tested for its ability to bind to an HGFR-like binding pocket. This may be achieved by testing the ability of the molecule to modulate HGFR activity using the assays described in Examples 3 and 4. Using this scheme, the synthesis of compounds with poor binding activities can be avoided.

[0145] A potential inhibitor of an HGFR-like substrate-binding domain may be computationally evaluated by means of a series of steps in which chemical entities or fragments are screened and selected for their ability to associate with the HGFR-like binding pockets. One skilled in the art may use one of several methods to screen chemical entities or fragments for their ability to associate with an HGFR-like substrate-binding domain. For example, one skilled in the art may visually inspect an HGFR-like substrate-binding pocket on a computer screen based on the HGFR structure coordinates reported in Table 1 or other coordinates which define a similar shape generated from the machine-readable storage medium. Selected fragments or chemical entities may then be positioned in a variety of orientations, or docked, within that binding pocket as defined *supra*. Docking may be accomplished using software such as Quanta and Sybyl, followed by energy minimization and molecular dynamics with standard molecular mechanics force fields, such as CHARMM and AMBER. Specialized computer programs to assist in the process of selecting fragments or chemical entities include the following:

1. GRID (Goodford, *J. Med. Chem.* 28:849-857 (1985)). GRID is available from the Oxford University, Oxford, UK.

2. MCSS (Miranker et al., *Proteins: Struct. Funct. and Genet.* 11:29-34 (1991)). MCSS is available from Accelrys, Inc., San Diego, CA.

3. AUTODOCK (Goodsell et al., *Proteins: Struct. Funct. and Genet.* 8:195-20 (1990)). AUTODOCK is available from the Scripps Research Institute, La Jolla, Calif.

4. DOCK (Kuntz et al., *J. Mol. Biol.*, 161:269-288 (1982)). DOCK is available from the University of California, San Francisco, CA.

5. GOLD (Jones et al., *J. Mol. Biol* 267:727-748 (1997)). GOLD is available from the Cambridge Crystallographic Data Centre, UK.

6. GLIDE (Eldridge et al., *J. Comput. Aided Mol. Des.* 11:425-445 (1997)). Glide is available from Schrödinger, Portland OR)

7. AGDOCK (Gehlahaar et al., *Chemsitry & Biol.* 2:317-324 (1995)). In-house software Agouron Pharmaceuticals, Inc./A Pfizer Co.

[0146] Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound or complex. Assembly may be preceded by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates of HGFR or an HGFR-ligand complex. This can be followed by manual model building using software such as Quanta or Sybyl (Tripos Associates, St. Louis, Mo.) Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include the following:

1. CAVEAT (Bartlett et al, *Molecular Recognition in Chemical and Biological Problems"*, Special Pub., Royal Chem. Soc., 78:182-196 (1989); Lauri et al., *J. Comput. Aided Mol. Des.* 8:51-66 (1994)). CAVEAT is available from the University of California, Berkeley, CA.

2. 3D Database systems such as ISIS (MDL Information Systems, San Leandro, Calif.). This area is reviewed in Martin, *J. Med. Chem.* 35:2145-2154 (1992)).

3. HOOK (Eisen et al, *Proteins: Struct., Funct., Genet.*, 19:199-221 (1994)). HOOK is available from Accelrys, Inc., San Diego, CA.

[0147] Instead of proceeding to build an inhibitor of an HGFR-like-binding pocket in a step-wise fashion one fragment or chemical entity at a time as described above, inhibitory or other HGFR-binding compounds may be designed as a whole or *de novo* using either an empty binding site or optionally including some portion(s) of a known inhibitor(s). There are many *de novo* ligand design methods including:

1. LUDI (H.-J. Bohm, *J. Comp. Aid. Molec. Design* 6:61-78 (1992). LUDI is available from Accelrys Incorporated, San Diego, Calif.

2. LEGEND (Y. Nishibata et al., *Tetrahedron* 47:8985 (1991). LEGEND is available from Accelrys Incorporated, San Diego, Calif.

3. LeapFrog (available from Tripos Associates, St. Louis, Mo.).

4. SPROUT (V. Gillet et al, *J. Comput. Aided Mol. Design* 7:127-153(1993). SPROUT is available from the University of Leeds, UK.

[0148] Other molecular modeling techniques may also be employed in accordance with this invention (see, e.g., N. C. Cohen et al., *J. Med. Chem.* 33:883-894 (1990); see also, M. A. Navia and M. A. Murcko, *Current Opinions in Structural Biology* 2:202-210 (1992); L. M. Balbes et al., *Reviews in Computational Chemistry,* Vol. 5, K. B. Lipkowitz and D. B. Boyd, Eds., VCH, New York, pp. 337-380 (1994); see also, W. C. Guida, *Curr. Opin. Struct. Biology* 4:777-781 (1994)).

[0149] Once a compound has been designed or selected by the above methods, the efficiency with which that entity may bind to an HGFR substrate-binding pocket may be tested and optimized by computational evaluation. For example, an effective HGFR substrate-binding pocket modulator must preferably demonstrate a relatively small difference in energy between its bound and free states (i.e., a small deformation energy of binding). HGFR substrate-binding pocket modulators may interact with the substrate-binding domain in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the energy of the free entity and the average energy of the conformations observed when the inhibitor binds to the protein.

[0150] An entity designed or selected as binding to an HGFR substrate-binding domain may be further computationally optimized so that in its bound state it would preferably lack repulsive electrostatic interaction with the target enzyme and with the surrounding water molecules. Such non-complementary electrostatic interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions.

[0151] Specific computer software is available in the art to evaluate compound deformation energy and electrostatic interactions. Examples of programs designed for such uses include: Gaussian (M. J. Frisch, Gaussian, Inc., Carnegie, PA); AMBER (P. A. Kollman, University of California at San Francisco); Jaguar (Schrödinger, Portland, OR); SPARTAN (Wavefunction, Inc., Irvine, CA); QUANTA/CHARMM (Accelrys, Inc., San Diego, CA.); Impact (Schrödinger, Portland, OR); Insight II/Discover (Accelrys, Inc., San Diego, CA); MacroModel (Schrödinger, Portland, OR); Maestro (Schrödinger, Portland, OR); DelPhi (Accelrys, Inc., San Diego, CA); and AMSOL (Quantum Chemistry Program Exchange, Indiana University). These programs may be implemented, for instance, using a Silicon Graphics workstation, such as an Indigo^2 with "IMPACT©" graphics. Other hardware systems and software packages will be known to those skilled in the art.

[0152] Another approach enabled by this invention, is the computational screening of small molecule databases for chemical entities or compounds that can bind in whole, or in part, to an HGFR substrate-binding pocket. In this screening, the quality of fit of such entities to the binding site may be judged either by shape complementarity or by estimated interaction energy (E. C. Meng et al. *J. Comp. Chem.* 13:505-524 (1992)).

[0153] Binding of potential inhibitors can also be assessed biochemically, for example, using isothermal titration calorimetry. See, e.g., Holdgate, *Biotechniques* 30:164-184 (2001).

[0154] According to another embodiment, the invention provides compounds that associate with an HGFR-like substrate-binding pocket produced or identified by the methods set forth above.

[0155] The structure coordinates of the invention as set forth in Table 1 can be used to obtain structural information about another crystallized molecule or molecular complex. This may be achieved by any of a number of well-known techniques, including molecular replacement. By using molecular replacement, all or part of the structure coordinates of the HGFR polypeptide-Compound 1 complex can be used to determine the structure of a crystallized molecule or molecular complex whose structure is unknown. Molecular replacement provides an accurate estimation of the phases for an unknown structure. Phases are a factor in equations used to solve crystal structures that cannot be determined directly. Obtaining accurate values for the phases, by methods other than molecular replacement, can be more time-consuming. Using molecular replacement methods, when the crystal structure of a protein containing at least a homologous portion has been solved, the phases from the known structure can provide an estimate of the phases for the unknown structure.

[0156] The method involves generating a preliminary model of a molecule or molecular complex whose structure coordinates are unknown, by orienting and positioning the relevant portion of the HGFR-Compound 1 complex according to Table 1 within the unit cell of the crystal of the unknown molecule or molecular complex so as best to account for the observed X-ray diffraction data of the crystal of the molecule or molecular complex whose structure is unknown. Phases can then be calculated from this model and combined with the observed X-ray diffraction data amplitudes to generate an electron density map of the structure whose coordinates are unknown. This, in turn, can be subjected to any known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallized molecule or molecular complex (E. Lattman, "Use of the Rotation and Translation Functions", in *Meth. Enzymol.*, 115, pp. 55-77 (1985); Rossmann, ed., "The Molecular Replacement Method", *Int. Sci. Rev. Ser.,* No. 13, Gordon & Breach, New York (1972)). Thus, the structure of any portion of any crystallized molecule or molecular complex that is sufficiently homologous to any portion of the HGFR/Ligand complex can be resolved by this method.

[0157] In another aspect, the method of molecular replacement is utilized to obtain structural information about another kinase. The structure coordinates of HGFR as provided by this invention are particularly useful in solving the structure of other isoforms of HGFR or other HGFR containing complexes.

[0158] Furthermore, the structure coordinates of HGFR as provided by this invention are useful in solving the structure of HGFR proteins that have amino acid substitutions, additions and/or deletions. These HGFR mutants may optionally be crystallized in co-complex with a chemical entity, such as a Compound 1 analogue. The crystal structures of the protein alone or a series of such complexes may then be solved by molecular replacement and compared with that of wild-type HGFR. Potential sites for modification within the various binding sites of the enzyme may thus be identified. This information provides an additional tool for determining the most efficient binding interactions, for example, in-

creased hydrophobic interactions, between HGFR and a chemical entity.

[0159] The structure coordinates of the invention are also useful to solve the structure of crystals of HGFR or HGFR homologues co-complexed with a variety of chemical entities. This approach enables the determination of the optimal sites for interaction between chemical entities, including potential HGFR modulators with the HGFR substrate-binding site. For example, high resolution X-ray diffraction data collected from crystals exposed to different types of solvent allows the determination of where each type of solvent molecule resides. Small molecules that bind tightly to those sites can then be designed and synthesized and tested for their ability to modulate HGFR activity.

[0160] All of the complexes referred to above may be studied using well-known X-ray diffraction techniques and may be refined versus X-ray data within a range of about 1.0 Å and about 3.0 Å to an R value of about 0.20 or less using computer software, such as X-PLOR (Yale University, distributed by Accelrys, Inc.; see, e.g., Blundell & Johnson, *supra*; *Meth. Enzymol.*, vol. 114 & 115, H. W. Wyckoff et al., eds., Academic Press (1985)). This information may be used to optimize known HGFR modulators, and to design new HGFR modulators.

EXAMPLES

Example 1: The HGFR Kinase Domain

1. Identification of the catalytic Domain Sequence

[0161] From the complete protein sequence for the human HGFR available from Swissprot: Locus MET_HUMAN, accession P08581, the sequence alignment programs (BLAST and ClustalW) were used to generate multiple sequence alignments with known kinases deposited in the PDB (Protein Data Bank containing deposited coordinates of solved protein structures). The alignments revealed that the insulin receptor tyrosine kinase domain (PDB: 1IR3-A) had the highest CLUSTAL-alignment score. Based on the insulin receptor and HGFR tyrosine kinase alignments, the baculovirus construct for the expression of human HGFR kinase domain (HGFRkd) was designed.

2. Cloning

[0162] The catalytic domain of the human HGFR kinase (HGFRkd) was cloned by PCR using Expand High Fidelity PCR System (Boehringer Mannheim) and Touchdown PCR (R.H. Don et al., *Nucleic Acids Research* 19: 4008 (1991)) from human liver and kidney Marathon-Ready cDNA (Clontech, Palo Alto, CA) with primers synthesized (Genset, La Jolla, CA) based on the published sequence [SEQ ID NO: 1]. The PCR oligonucleotide primer sequences are listed below in Table 2.

Table 2. PCR Primers

Primer	Sequence
MetF	5' GATCCCATGGTCCACATTGACCTCAGTGCTC 3' [SEQ ID NO 6]
MetR	5' CTAGAAGCTTCTAGTGCTCCCCAATGAAAGTAGAGAAGAT 3' [SEQID NO 7]

3. Expression and Purification of Recombinant HGFR Kinase

[0163] The cDNA corresponding to residues 1051-1349 of the HGFR kinase catalytic domain (HGFRkd) was cloned into a pFastBac plasmid (Life Technologies) modified by the introduction of an *Nco*I site. A recombinant baculovirus was generated using the Bacmid system (Life Technologies). The protein was expressed in SF-9 insect cells (Invitrogen, Carlsbad, CA) and purified by conventional column chromatography.

4. Generation of Expression Plasmids

[0164] Plasmid pFastBac-*Nco*I was modified from the pFastBac1 vector (Life Technologies, Gaithersburg, MD) by *in vitro* site-directed mutagenesis using the QuickChange™ site-directed mutagenesis method (Stratagene, La Jolla, CA). The nucleotide sequence in the vector AATATTCCG was mutated to ACCATGCCG to create a unique *Nco*I site at the original translation start site for the polyhedrin protein. The amplified cDNA fragment was ligated into TopoII PCR vector (Invitrogen) and the recombinant plasmid amplified. The cDNA fragment corresponding to the *Met* kinase domain

was excised from the TopoII PCR vector with the restriction enzymes *Nco*I and *Hind*III and subcloned into *Nco*I and *Hind*III digested pFastBac-*Nco*I. Recombinant PfastBac-*Nco*I clones containing the *Met* kinase domain were sequence-verified.

5. Generation of Recombinant Virus

[0165] The Bac-to-Bac system (Life Technologies) was used to generate recombinant baculovirus for expression of the *Met* kinase. Recombinant virus was confirmed by PCR for the presence of the *Met* kinase encoding insert. SDS-PAGE or Western blot analysis with anti-*Met* polyclonal antibodies confirmed protein expression. 2-3 rounds of amplification in SF9 insect cells generated high titer stocks of recombinant virus.

6. Expression in Insect Cells

[0166] The titer of the virus stock was 1 to 5 x10^8 p.f.u./ml. The viral titration was determined by the plaque assay method, with serial 10-fold dilution up to 10^8-fold. The viral stock was used for large-scale protein production. Sf9 cells were grown in upright roller bottles up to a cell density of 2x10^6 and subsequently used as seed cells for bioreactor culture. The cells were grown in a 20 L stirred bioreactor with working volume at 18L (Applikon Inc., Foster City, CA). Routinely, the MOI varied from 3-5 and the infection was carried out for 48 hours. After 48 hrs of infection, the infected cells were harvested by centrifugation at 3,000 rpm for 10 min at 4°C. Cell pellets were collected and stored at -80°C.

7. Purification of HGFR kinase catalytic domain (HGFRkd)

[0167] The basic purification scheme is depicted in Figure 1. Frozen cell pellets were thawed, suspended in ice-cold lysis buffer, and lysed by microfluidization (Microfluidics Corp, Newton, MA). All steps were performed at 4°C. A detailed protocol follows:

Buffer A: 50 mM Tris-Cl, pH 7.8, 150 mM NaCl, 5 mM DTT, 10% glycerol.
Buffer B: 50 mM MES pH 6.5, 150 mM NaCl, 3 mM DTT, 10% glycerol.
Buffer C: 50 mM MES pH 6.5, 0.6 M $(NH_4)_2SO_4$, 3 mM DTT.
Buffer D: 50 mM MES pH 6.5. 50 mM NaCl, 3 mM DTT.
Buffer E: 50 mM MES pH 6.5, 50 mM NaCl, 3 mM DTT, 10% glycerol.

[0168] Cell pellets (approx. 50 to 60 grams) were resuspended in 4 x volume of buffer A (50 mM Tris-Cl, pH 7.8, 150 mM NaCl, 5 mM DTT, 10% glycerol). 6 ml of PIC (Protease Inhibitor Cocktail, Sigma) was added to the resuspension and the cells were lysed by passing the solution through the high pressure microfluidizer (Microfluidics Corp, Newton, MA) once. The lysate was cleared at 40,000 rpm, 4°C for 45 min by ultracentrifugation (Beckman Optima LE-80K Ultracentrifuge). The cleared supernatant was loaded onto a Q-FF Sepharose column (Pharmacia XK50/20, 150 ml) equilibrated in buffer A at a rate of 10 ml/min.

[0169] The Q-FF Sepharose flow-through was loaded onto an equilibrated G-25 column (Pharmacia XK50/60, 1000 ml) in buffer B (50 mM MES pH 6.5, 150 mM NaCl, 10% glycerol, 3 mM DTT) at a flow rate of 20 ml/min. Combined flow-through fractions from the G-25 column were pooled and applied to an Heparin-Sepharose column (Pharmacia XK 26/20, 60 ml) equilibrated in buffer B. The pool from the G-25 column was loaded onto the Heparin-Sepharose column at 8 ml/min. The column was washed with 300 ml of buffer B and the protein eluted with a 600 ml salt linear gradient spanning from 150 mM NaCl to 600 mM NaCl at 4 ml/min. 8 ml fractions were collected and analyzed by SDS-PAGE. Fractions containing the recombinant *Met* kinase domain (~34,000 Dalton) were collected and pooled.

[0170] The pool from the Heparin-Sepharose column was adjusted to a final concentration of 0.6 M ammonium sulfate by the addition of 4 M ammonium sulfate to the slowly stirred solution at 4°C for 30 min. After addition of the ammonium sulfate, the solution was applied to a Phenyl-Sepharose column (Pharmacia XK 16/20, 20 ml) equilibrated in buffer C (50 mM MES pH 6.5, 0.6 M $(NH_4)_2SO_4$, 3 mM DTT) at a flow rate of 4 ml/min. The column was washed with 100 ml of buffer C and the protein eluted with a 400 ml gradient from 100% buffer C to 100% buffer D (50 mM MES pH 6.5. 50 mM NaCl, 3 mM DTT). The column was further washed with 100 ml of 100% buffer D. 6 ml fractions were collected and analyzed by SDS-PAGE prior to pooling fractions containing the recombinant *Met* kinase domain. The pooled fractions were dialyzed against 4 liters of buffer E (50 mM MES pH 6.5, 50 mM NaCl, 10% glycerol, 3 mM DTT) at 4°C overnight.

[0171] The dialyzed pool was filtered through a 0.2 μm filter prior to loading onto an equilibrated (buffer E) mono S column (Pharmacia, mono S HR 10/10, 7.8 ml) using the FPLC system (Pharmacia). The sample was loaded at 2 ml/min. The column was washed with 40 ml of buffer E and the protein eluted with a linear 160 ml salt gradient from 50 mM NaCl to 300 mM NaCl at 2 ml/min. 2 ml fractions were collected and analyzed by SDS-PAGE prior to pooling.

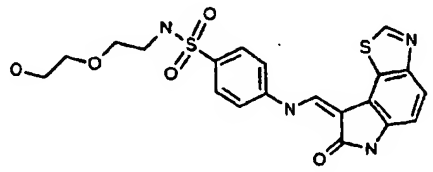
[0172] A Superdex 75 gel filtration column (Pharmacia, Superdex HiLoad 16/60, 120 ml) was equilibrated in buffer B. The pool from the mono S column was concentrated to less than 2 ml and the protein sample injected into the column using a FPLC unit. The column was developed with 120 ml of buffer B and 1.5 ml fractions were collected. The monomeric peak was collected and analyzed by SDS-PAGE. The protein at this stage is ~98% homogenous. The monomeric fraction corresponding to purified *Met* kinase domain (HGFRkd) was concentrated to 6-7 mg/ml for crystallization trials or 5 mg/ml for high-throughput screening (HTS). Alternatively, protein was flash-frozen in liquid N_2 for long-term storage at -80°C.

Example 2: Crystalization, Crystallography and Three-Dimensional Analysis

1. HGFRkd [SEQ ID NO. 4]-Compound **1** crystallization

[0173] Extensive screening of crystallization conditions was performed to produce crystals of HGFRkd. Successful crystallization of HGFRkd was performed by first incubating unphosphorylated HGFRkd with Compound **1** (4-[[(Z) -(6,7-dihydro-7-oxo-8H-pyrrolo[2,3-g]benzothiazol-8-ylidene)methyl]amino]-N-[2-(2-hydroxyethoxy)ethyl]-(9Cl).

[0174] Compound **1**, which is represented by the following formula, can be prepared in accordance with International Publication No. WO 99/15500, which is hereby incorporated by reference in its entirety:



[0175] Compound **1** (using a stock solution of 70mM Compound **1** dissolved in dimethyl sulfoxide) was added in a 5:1 molar ratio of Compound **1** to HGFRkd to a solution containing: HGFRkd at a concentration of 6-7 mg/mL, 25mM 2-Morpholinoethanesulfonic acid monohydrate at pH 6.5, 150mM NaCl, and 2mM dithiothreitol. After **1** hour the solution was microfuged to remove any undissolved particles and the solution was mixed with an equal volume of precipitating solutions containing: 27-34% monomethylether polyethylene glycol (average molecular weight 350Da and 50 mM 4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid at pH 7.5). Using the hanging-drop diffusion method of protein crystallization (Matthews, B.W. (1968). *J. Mol. Biol.* 33, 491-497), 4 µL of the above solution was dispensed onto glass coverslips, inverted, and sealed over a reservoir containing 0.5 - 1.0 mL of the precipitating solution. Crystals of average dimensions 0.4 x 0.4 x 0.05mm grew over 3-5 days at a temperature of 23°C.

2. HGFRkd-Compound **1** X-ray diffraction data collection

[0176] Two X-ray diffraction data sets were generated and used to solve the three-dimensional structure of the HGFRkd-Compound **1** complex. A 1.9 Å resolution data set was collected using a Rigaku rotating anode X-ray generator (CuKα) and a MAR345 MAR Research image plate detector. A 1.22 Å resolution data set was collected at the Stanford Sunchrotron Radiation Light-source (SSRL) using beam-line 7.1. During both data collections the crystals were kept frozen in a stream of liquid nitrogen. The observed data sets were processed with versions of the programs DENZO and SCALEPACK (Otwinowski, Z. (1993). Oscillation data reduction program. In *Proceedings of the CCP4 Study Weekend: Data Collection and Processing.* (Sawyer, L., Isaacs, N., & Bailey, S., eds), pp. 56-62, SERC Daresbury Laboratory, England). Processing of the data revealed the crystals to belong to the P2(1) crystallographic space group with approximate unit cell constants of a = 37.8 Å, b = 41.6 Å, c = 88.0 Å, alpha = 90°, beta = 92.6°, and gamma=90.0°.

3. HGFRkd-Compound **1** three-dimensional structure determination

[0177] The approximate rotational and translational position of HGFRkd in the crystal lattice was solved using the program EPMR (Kissinger, C. and Gehlhaar, D (1999). EPMR: A program for crystallographic molecular replacement by evolutionary search. Agouron Pharmaceuticals, Inc., 11099 N. Torrey Pines Rd., La Jolla, CA 92037-1020), a model composed of parts of the structure of lymphocyte kinase (Yamaguchi, H. & Hendrickson, W. A. (1996). Structural basis for activation of human lymphocyte kinase Lck upon tyrosine phosphorylation. *Nature* 384, 484-489, Brookhaven Protein Data Bank entry 3lck) and the 1.9 Å HGFRkd-Compound 1 diffraction data set. The probe model was generated by removing residues of the non-conserved N-terminus, kinase activation loop, and kinase insert region of Lck. After

the approximate position of HGFRkd was determined, the individual atomic positions of HGFRkd were fit using the 1.22 Å diffraction data set and the programs *wARP* (Perrakis, A., Morris, R., & Lamzin V. S. (1999) *Nature Struct. Biol.* 6, 496-500) and *SHELXL* (Sheldrick, G. M. & Schneider, T. R. (1997). *Methods Enzymol.* 277, 319-343) with manual fitting to electron density maps. The refined model has an R-factor of 0.1355 calculated using all of the data.

4. Description of the HGFRkd-Compound **1** Three-Dimensional (3-D) Structure

Structural Overview

[0178] The overall structure of HGFRkd-Compound **1** is similar to that reported for other kinases, however HGFRkd contains unique features. As in other protein kinase structures, the protein is folded into two domains with ATP binding and phosphotransfer occurring in the cleft between the two domains (reviewed in Cox, S., Radzio-Andzelm, E. & Taylor, S. S. (1994). Domain movements in protein kinases. *Curr. Opin. Struct. Biol.* 4, 893-901). Figure 2 depicts the overall fold of HGFRkd with secondary structural elements assigned according to the convention originally given for cyclic AMP-dependent protein kinase (cAPK) (Knighton et al., *Science* 253:407-413 (1991)). The HGFRkd 3-D structural model extends over the range of residues leucine1062 through histidine 1348.

[0179] Of the published protein kinase structures, the overall structure of HGFRkd appears to follow most closely those of the insulin receptor kinase (IRK) (Hubbard et al., *Nature* 372:746-754 (1994); Hubbard et al., *Embo J.* 16: 5572-5581 (1997)). Certain regions of HGFRkd share more similarity to IRK and other regions follow the phosphorylated IRK (pIRK) structure more closely. While regions of HGFRkd fold share similarity to the IRK and pIRK, the HGFRkd has unique structural elements. For simplicity, the structural differences will be described beginning at the N-terminus.

[0180] Residues 1062-1067 form a short helix that does not occur in IRK, IRKP, or in other reported receptor tyrosine kinase structures (McTigue et al., *Structure* 7, 319-330 (1999); Mohammadi et al., *Science* 276:955-960 (1997)). Residues 1079-1082 are an insertion in beta strand 1 relative to IRK and other kinases. This insertion results in a kink in beta strand 1. The position of the glycine-rich loop (residues 1085-1092) follows IRKP much more closely than IRK. The apex of the loop (phenylalanine 1089), however, has a very different conformation from IRKP. Relative to IRKP, Phe 1089 is inserted farther towards alpha helix C and thus affects the position of alpha helix C. The axis of alpha C is approximately 23° farther from the protein core than in IRKP and residues 1113- 1121 at the end of beta strand 3 and the beginning of alpha helix C are disordered (do not have a discreet position) in HGFRkd. The turn between beta strands 4 and 5 (residues 1149 -1152) is disordered in HGFRkd. This disorder, relative to other kinase structures, may be due to the insertion of an additional residue in this turn in HGFR. The kinase insert domain of HGFRkd (residues 1172-1178) folds differently than in other kinase structures. In HGFRkd the kinase insert domain is relatively short and forms an extended loop between alpha helix D and alpha helix E. Following the kinase insert domain the backbone of alpha helix E, the catalytic loop, and beta strands 7 and 8 superimpose reasonably with IRKP. The HGFRkd structure then diverges significantly from other kinase structures in the activation loop region (residues 1221-1244), discussed in more detail below. The rest of the HGFRkd backbone fold follows the same general path as IRKP until alpha helix I. In HGFRkd alpha helix I is oriented so that the C-terminal tail (residues 1342-1348) following this helix veer towards and packs against the kinase insert domain.

Kinase activation loop conformation

[0181] The kinase activation loop (residues 1221-1244) in HGFRkd has a unique inhibitory conformation that prevents ATP binding, peptide substrate binding, affects the position of alpha helix C, and creates a unique binding site for inhibitors. At the beginning of the loop, residues 1223-1227 form a sharp turn or knob that juts into alpha helix C and appears to distort this helix at the point of contact, glycine 1128 (Figure 2). After glycine-1128 residues 1129-1134 are distorted from a normal alpha helix geometry into a 3_{10} helical geometry. The insertion of residues 1223-1227 towards alpha helix C may also be responsible for pushing this helix away from the protein core and thus away from proper positioning for catalysis. The sidechain of aspartic acid 1228 points towards the glycine-rich loop and appears to force phenylalanine 1089 to adopt a position which would interfere with the correct positioning of alpha helix C for catalysis. The position of tyrosine 1230 occupies the triphosphate binding site of ATP and thus prevents proper ATP binding. The backbone of residues 1234-1238 adopts a position similar to that of the peptide substrate in the IRKP structure, and thus the position of these residues is inhibitory to peptide substrate binding.

Inhibitor binding site

[0182] A depiction of the Compound **1** binding site is shown in Figures 3 and 4. The hydroxyethoxymethyl group of Compound **1** is not included in the 3-D structure as the electron density for this group is ambiguous, suggesting that this group adopts many different conformations. The binding site of Compound **1** roughly superimposes with the pre-

dicted binding site for the adenine group of ATP. The site is located in a cleft between parts of the N and C-terminal kinase domains (Figure 1). Residues of HGFRkd that form the site include: 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231. The oxopyrrolo of Compound 1 makes hydrogen bonds to the amino of methione 1160 and the carbonyl of proline 1158. These hydrogen bonds are analogous to those reported in structures of indolinones bound to the fibroblast growth factor receptor kinase (Mohammadi et al., *Science* 276:955-960 (1997)) and cyclin-dependent kinase 2 (Davis et al., *Science* 291:134-137 (2001)). The unique conformation of the kinase activation loop, particularly residues 1226-1231, contributes substantially to the uniqueness of the inhibitor site seen in this HGFRkd structure.

Example 3: HGFR Biochemical Characterization

1. Materials

[0183] γ-[^{32}P]-ATP was purchased from Pharmacia-Amersham. GF/B glass fiber filterplates and Microscint-20 were purchased from Packard. The following reagents were purchased from the Sigma Chemical Company: poly(Glu_4Tyr), dephosphorylated α-casein, lactate dehydrogenase, pyruvate kinase, phosphoenolpyruvate, HEPES (N-[2-hydroxyethyl]piperazine-N'-[4-butanesulfonic acid]), MOPS (3-[N-morpholino]propanesulfonic acid), MES (2-[N-morpholino] ethanesulfonic acid), Bis-Tris Propane (BTP; 1,3-bis[tris(hydroxymethyl)methylamino]propane), NaCl, dithiothreitol, $MgCl_2$, ATP, and NADH. Met2 peptide (Ac-ARDMYDKEYYSVHNK [SEQ ID NO. 8]) was synthesized on a ABI 433A peptide synthesizer and purified to >95% purity by HPLC.

2. Enzymatic Assays

[0184] A coupled enzymatic assay format was used to measure both HGFR and phospho-HGFR (pHGFR) activities. The kinase-catalyzed production of ADP from ATP that accompanies phosphate transfer to the random copolymer poly (Glu_4Tyr) or peptide substrate was coupled to the oxidation of NADH through the activities of pyruvate kinase (PK) and lactate dehydrogenase (LDH). NADH conversion to NAD^+ was monitored by the decrease in absorbance at 340 nm (ε = 6.22 $cm^{-1}mM^{-1}$) using a Beckman DU650 spectrophotometer. A typical reaction solution contained 1 mM phosphoenolpyruvate, 0.24 mM NADH, 40 mM $MgCl_2$, 5 mM DTT, poly(Glu_4Tyr), ATP, 15 units/mL PK, 15 units/mL LDH in 100 mM HEPES, pH 7.5. ATP was varied from 0.5 to 2000 μM and poly(Glu_4Tyr) was varied from 0.5 to 20 mg/mL. In addition, Met2 peptide (0-4 mM) could be used instead of poly(Glu_4Tyr). Assays were initiated with the addition of 12 nM phosphorylated HGFR or 125 nM unphosphorylated HGFR. Inhibition studies were performed as described above with following exceptions: 0.075 mM ATP (pHGFR) and 0.375 mM ATP (HGFR). Data was fit to the equation for competitive inhibition by the method of nonlinear least squares (KaleidaGraph).

[0185] A second assay format was used to monitor the production of the other kinase product: phospho-protein. This simple radioactive assay was used to monitor the transfer of phosphate from γ-[^{32}P]-ATP to dephosphorylated α-casein. The glass fiber filterplate assay format measures the capture of TCA-precipitated [^{32}P]-phosphorylated proteins on glass fiber filters in a 96-well format. The kinetic parameters for HGFR were evaluated in the filtermate assay format and were similar to the values determined in the coupled enzymatic format. Typical assay conditions for measuring inhibition were established: 27.5 nM pHGFR, 0.075 mM ATP, 0.0109 mM dephosphorylated α-casein, 0.5 μCi γ-[^{32}P] -ATP, 20 mM $MgCl_2$, 2 mM DTT, 100 mM HEPES pH 7.5, 0.10 mL, RT, and 30 min. These conditions deliver a signal/noise ratio greater than 20.

3. HGFR Autophosphorylation

[0186] Typical autophosphorylation reactions to produce maximally active pHGFR were performed at 4°C for 4 hours with the following components: 10 μM HGFR, 100 mM HEPES (pH 7.5), 20 mM $MgCl_2$, 4 mM ATP, and 2 mM DTT. At fixed time points in the autophosphorylation reaction, the extent of autophosphorylation was measured for enhancement of kinase activity: coupled enzymatic assay with 2 mM ATP, variable poly(Glu_4Tyr) (0, 0.38, 0.76, 1.5, 3, 6 mg/mL). The extent of autophosphorylation was also measured by isoelectric focussing gel electrophoresis (IEF) analysis (5 μg/ time point). Finally, mass spectrometry was used to identify the site of phosphate incorporation into HGFR.

4. Mass Spectrometry

Proteolysis experiments.

[0187] Unphosphorylated and phosphorylated HGFR samples were digested by trypsin (100ng) overnight in a 100 mM ammonium bicarbonate/30% acetonitrile/3mM Tris-HCl buffer (pH 8) at 37°C. The tryptic peptides were extracted

out of the gel using 50% acetonitrile/ 0.1% TFA, concentrated to 10 µl, and subjected to MALDI and nanoESI mass analysis.

MALDI/MS analysis.

[0188] All MALDI-MS analyses were performed in a Voyager-Elite; time-of-flight mass spectrometer with delayed extraction (PerSeptive Biosystems, Inc., Framingham, MA). A volume of 1 µl of digested protein was placed directly on the MALDI analysis plate, mixed with 1 µl of matrix (α-cyano-4-hydroxy-cinnamic acid) in a saturated solution of acetonitrile/water (50:50, v/v) with 0.1% (w:w) trifluoroacetic acid (TFA) and inserted into the MALDI ionization source for analysis. Samples were irradiated with a nitrogen laser (Laser Science Inc.) operated at 337nm. The laser beam was attenuated by a neutral density filter onto the sample target. Ions produced by laser desorption were typically energetically stabilized during a delayed extraction period of 150 nanoseconds and were then accelerated through the time-of-flight mass analyzer with a 20 kV potential. Spectra shown were typically an average of 128 laser pulses.

NanoESI-MS.

[0189] MS/MS analyses were performed on a triple quadrupole mass spectrometer (PE Sciex API III, Alberta, Canada) modified with a nanoESI source from Protana A/S, (Denmark). The ESI voltage was set at 850 V and the orifice settings were maintained at 100 V. A curtain gas of ultrapure nitrogen was pumped into the interface at a rate of 0.6 L/min to aid evaporation of solvent droplets and to prevent particulate matter from entering the analyzer. For precursor ion scan experiment, 3µl of digested protein was mixed with 3µL 25 mM ammonia solution and 3µL methanol (pH=9). For product ion scan experiment, 3 µL of digested protein was mixed with 7µl of methanol and 0.5 µL formic acid. A 4 µL aliquot was loaded into a palladium-coated borosilicate glass capillary and injected into mass spectrometer. Precursor ion scanning was used to generate spectra of its precursors (or "parent" ions) of the phosphate fragment *m/z* 79. Product ion scan was also used to obtain the sequence information of phosphopeptides.

5. Results

Autophosphorylation of HGFR

[0190] HGFR was activated through an autophosphorylation reaction to produce phospho-HGFR (pHGFR). To achieve high specific activity pHGFR, large-scale autophosphorylation reactions were performed at high HGFR concentration (typically 10 µM), high ATP concentration (4 mM), and low temperature (4°C). The extent of the reaction was monitored by native isoelectric focussing electrophoresis (IEF) with both Coomassie staining for protein (Figure 5(A)) and [^{32}P]-phosphate incorporation by autoradiography (Figure 5(B)) with small 0.05mL reactions at 20°C. In addition, quantitation of HGFR activity as a function of autophosphorylation time was performed to optimize the reaction in terms of catalytically relevant autophosphorylation. IEF analysis revealed that the HGFR kinase domain was a single species with pI = 7.9 (Figure 5(A)). Limited autophosphorylation shifted HGFR to a second species with pI = 6.6 (Figures 5(A) and 5(B)). Further autophosphorylation shifted HGFR to a third species (pI = 7.2). The enhancement in catalytic efficiency increased as a function of autophosphorylation time. A larger scale reaction (1 mg) was performed at 4°C to produce pHGFR for kinetic studies (Figure 5(C)). Although sequential phosphorylation events can be inferred by the IEF analysis, the precise assignment of these sites was not possible. As such, the determination of the phosphorylation sites and order of phosphate incorporation was investigated by mass spectrometric analysis.

Determination of Phosphorylation Sites on HGFR.

[0191] A preliminary investigation into the HGFR autophosphorylation sites was performed with samples of HGFR and fully phosphorylated HGFR (pHGFR). The samples were proteolyzed with trypsin and subjected to MALDI-TOF mass spectrometry, the results of which are shown in Figure 5(D). One major phosphorylation site was identified. The major phosphopeptide corresponded to HGFR residues 1233-1240 (SYYSVHNK) which is contained in the HGFR activation loop. Parent ion scans using nano-spray EI mass spectrometry, shown in Figure 5(E), confirmed the identified sites. Tyrosine 1235 has been shown to be autophosphorylated (Ferracini, R., Longati, P., Naldini, L., Vigna, E., and Comoglio, P. M. (1991) *J. Biol. Chem 266,* 19558-19564).

Kinetic Analysis of HGFR and pHGFR

[0192] The kinetic consequences of the autophosphorylation were investigated. HGFR and pHGFR activities were evaluated in two distinct and complementing assay formats. Autophosphorylation of HGFR was shown to occur on the

activation loop and enhances the kinase specific activity. A coupled, enzymatic assay format (CE format) was used to measure ADP production. HGFR-catalyzed production of ADP from ATP that accompanied phosphate transfer to the random copolymer poly(Glu_4Tyr) was coupled to the oxidation of NADH through the sequential activities of pyruvate kinase (PK) and lactate dehydrogenase (LDH). NADH conversion to NAD^+ was monitored spectrophotometrically by the decrease in absorbance at 340 nm ($\varepsilon = 6.22\ cm^{-1}mM^{-1}$). A second assay format was used to measure the production of [^{32}P]-labeled phospho-protein (dephosphorylated α-casein). Dephosphorylated α-casein is the substrate for HGFR in the coupled enzymatic format and in a glass fiber filterplate assay format. The $K_{m,Dephosphorylated\ \alpha\text{-}casein}$ was determined to be 28.5 ± 3.5 μM in the coupled, enzymatic format. The filtermate assay format is as follows: kinase reactions run with γ-[^{32}P]-ATP, dephosphorylated α-casein phosphoacceptor, terminated with trichloroacetic acid, and isolated on glass fiber 96-well filterplates. Both assays produced similar K_m values for ATP: 73.7 ± 2.8 μM (coupled enzymatic format) and 78.6 ± 12.1 μM (radioactive filtermate format). By monitoring activity with the coupled enzymatic assay, autophosphorylation of HGFR caused a 32-fold enhancement in turnover number (k_{cat}) and 164-fold enhancement in the specificity constant (k_{cat}/K_m) (Table 3). Minor changes in substrate K_m values between HGFR and pHGFR were observed (Table 3). As determined in multiple assays with multiple phosphoacceptor substrates, autophosphorylation transformed HGFR into a much more potent catalyst (pHGFR).

Inhibition of HGFR and pHGFR

[0193] Inhibition of HGFR and pHGFR were monitored in two distinct assay formats to insure valid results. The coupled, enzymatic format (CE) was a continuous assay that measured ADP production through the sequential action of two standard coupling enzymes (pyruvate kinase and lactate dehydrogenase). The radioactive assay format was a discontinuous assay that measured phospho-protein production directly. As part of the assay validation, the inhibition of staurosporine was measured: 132 ± 6 nM (pHGFR/CE format), 97 ± 7 nM (pHGFR/radioactive format), and 260 ± 16 nM (HGFR/CE format). As expected, the general kinase inhibitor staurosporine was a potent HGFR and pHGFR inhibitor. Compound **1** was tested in both assay formats against both HGFR and pHGFR: 128 ± 17 nM (pHGFR/radioactive format), 381 ± 19 nM (pHGFR/CE format), and 500 ± 30 nM (HGFR/CE format). The inhibition of HGFR and pHGFR by Compound **1** as measured in the coupled enzymatic assay is shown in Figure 6(A). To determine the mechanism of pHGFR inhibition by Compound **1**, double reciprocal analysis was undertaken. In the CE assay, ATP (25, 50, 75, 100, 200, 400, 800, 1600, 3200 μM) and Compound **1** (0, 150, 300, 1200 nM) were varied at fixed concentrations of pHGFR (25 nM) and Met2 peptide (0.5 mM). The resulting family of lines had a common y-intercept (1/Vmax) and different slopes (Figure 6(B)). This result is consistent with Compound **1** being an ATP-competitive inhibitor of pHGFR. As measured in both formats, Compound **1** is a potent HGFR and pHGFR inhibitor.

6. Discussion

Autophosphorylation Site

[0194] Receptor autophosphorylation is an essential event in many signal transduction pathways and is known to have multiple functions *in vivo* including activation of the kinase domain and creation of recruitment sites for downstream signaling molecules. For many RTKs multiple sites are phosphorylated and the order of phosphorylation of these sites can be either random or sequential. Receptor kinase domains are usually activated by phosphorylation of a tyrosine residue in the activation loop (Hubbard, S. R., and Till, J. H. (2000) *Annu Rev Biochem 69*, 373-98). Autophosphorylation of HGFR results in the enhancement in kinase activity concomitant with the phosphorylation of the activation loop. Furthermore, the identified activation loop sequence contains the reported HGFR autophosphorylation site: Y1235 (Ferracini, R., Longati, P., Naldini, L., Vigna, E., and Comoglio, P. M. (1991) *J. Biol. Chem 266,* 19558-19564). The insulin receptor has been shown to autophosphorylate in the activation loop on three tyrosine residues (White, M. F., Shoelson, S. E., Keutmann, H., and Kahn, C. R. (1988) *J Biol Chem 263,* 2969-80).

Kinetic Analysis of HGFR and pHGFR

[0195] The autophosphorylation can be either cis (intramolecular) or trans (intermolecular). In the trans mechanism, the receptor dimerization increases the effective concentration of the kinase domains which enhances the reaction rate. The HGFR autophosphorylation rate is dependent on the concentration of HGFR. This observation is consistent with a trans autophosphorylation mechanism. Other RTK such as the insulin receptor (Hubbard, S. R., Wei, L., Ellis, L., and Hendrickson, W. A. (1994) *Nature 372*, 746-54; Hubbard, S. R. (1997) *Embo J 16*, 5572-81) and VEGF receptor (Parast, C. V., Mroczkowski, B., Pinko, C., Misialek, S., Khambatta, G., and Appelt, K. (1998) *Biochemistry 37,* 16788-801) have been shown to have a *trans* mechanism for autophosphorylation of the activation loop.

[0196] Kinetic analysis of unphosphorylated and autophosphorylated HGFR was undertaken to probe the overall

effect of autophosphorylation on the effectiveness and efficiency of HGFR as a catalyst. As observed for other receptor tyrosine kinases, HGFR and pHGFR are robust kinases. The k_{cat} value for HGFR increases from 1.02 s^{-1} to 31.3 s^{-1} after autophosphorylation (30-fold enhancement). For example, the VEGFR2 receptor tyrosine kinase has high turnover numbers for both unphosphorylated (k_{cat} = 5 s^{-1}) and autophosphorylated (k_{cat} = 12 s^{-1}) forms. Though the primary effect of autophosphorylation resides on k_{cat}, there is a K_m effect. The substrate specificity constant (k_{cat}/K_m) for both HGFR (165-fold) and VEGFR2 (10-fold) is increased significantly as a result of autophosphorylation. Others have shown a 7-fold V_{max} enhancement of HGFR *(c-Met)* (Naldini, L., Vigna, E., Ferracini, R., Longati, P., Gandino, L., Prat, M., and Comoglio, P. M. (1991) *Mol Cell Biol 11*, 1793-803). The insulin receptor has a large 200-fold increase in specific activity as a result of autophosphorylation (Wei, L., Hubbard, S. R., Hendrickson, W. A., and Ellis, L. (1995) *J Biol Chem 270,* 8122-30). It should be noted that the tyrosine residue in the activation loop of the EGF receptor has not been shown to contribute to receptor activation (Gotoh, N., Tojo, A., Hino, M., Yazaki, Y., and Shibuya, M. (1992) *Biochem Biophys Res Commun 186*, 768-74). HGFR is a potent kinase that undergoes a large enhancement in activity due to autophosphorylation.

Table 3

	Unphosphorylated HGFR			Phospho-HGFR		
	K_m (μM)	k_{cat} (s^{-1})	k_{cat}/K_m ($s^{-1}M^{-1}$)	K_m (μM)	k_{cat} (s^{-1})	K_{cat}/K_m ($s^{-1}M^{-1}$)
MgATP	373 ± 61	1.02 ± 0.013	2730	73.7 ± 2.8	31.3 ± 2.1	449,000
Poly(Glu_4Tyr)	10080 ± 260		48.1	8194 ± 651		9,260

[0197] As seen in the data of Table 3, autophosphorylation of HGFR enhances its catalytic efficiency. The observed enhancement was independent of phosphoacceptor and assay format as measured by steady-state kinetic constants for HGFR and autophosphorylated HGFR. The coupled enzymatic analysis of HGFR processing of ATP and poly (Glu_4Tyr) were measured at 37°C. Variable substrate concentration was measured at a fixed saturating concentration of the other substrate.

Example 4. Screening-Biochemical and Cell Based Assays: DELIFA HTS (DELIFA High Throughput Screen)

[0198] This is a 384-well plate DELFIA assay, a time-resolved fluorescence (TRF) assay for the HGFR kinase. In this assay, the kinase is assayed at room temperature on a Neutravidin-coated white 384-well plate using biotin-gastrin as the peptide substrate in the presence of ATP and with or without inhibitors. The reaction is stopped; the plate is washed and then incubated with europium (Eu) labeled antiphosphotyrosine antibody (anti-PY-Eu Ab), which binds to the phosphotyrosine product. The plate is washed and then incubated with an enhancement solution followed by plate read in a fluorescence plate reader under Eu time-resolved settings to quantify the amount of anti-PY-Eu bound. The Eu counts are directly proportional to the HGFR kinase activity.

1. Assay Protocol

Materials and Reagent

[0199]

- 384-well flat bottom NeutrAvidin coated microtitre plates (Pierce)
- Substrate: biotin-Gastrin(American Peptide Co.). Stock 10 mM made in DMSO (not very soluble in water)
- HGFR kinase (autophosphorylated, stored at -80°C)
- Anti-PY-Eu antibody (Wallac)
- 1X Enhancement solution (Wallac)
- TBS/Tween-20 (0.05%)
- Antibody diluent: TBS / Tween-20 + 10 mg/ml BSA (Fraction-V, ELISA grade Calbiochem, Cat # 126593)
- ATP (Sigma); Tris (Sigma); $MgCl_2$ (Fisher); DTT (Calbiochem); NaCl (Fisher); DMSO (Fisher)
- Victor plate reader

Stock Solutions (in distilled water, unless otherwise stated)

[0200] 1.0 M HEPES (pH 8); 1.0 M $MgCl_2$; 2.0 M NaCl; 1.0 M DTT; 0.5 M ATP; 10 mM biotin-Gastrin; 10X TBS/

Tween-20; 10X Ab diluent; 50X inhibitor controls in DMSO.

Reaction Mixture	Assay Buffer
100 mM HEPES 2 mM DTT 20 mM $MgCl_2$ 25 mM NaCl 100 μg/ml BSA	100 mM HEPES 2 mM DTT 20 mM $MgCl_2$

Inhibitor controls: Starosporin at 10 μM and 1 μM.

2. Assay Plate Format and Screening Conditions

[0201]

Assay Volume	50 μl
pH	7.5
HGFR kinase	0.75 nM
Biotin-gastrin	1 μM
ATP	75 μM
Inhibitor controls	Starosporin at 2 μM, 0.5 μM, and 0.4 μM
Compounds	10 μM
Reaction time	11 min

3. 96-Well Plate Set-Up (same set up for each quadrant of a 384-well plate)

[0202]

a) Columns 1-11, test compounds
b) Column 12, controls: wells A12, B12, C12 are DMSO controls; well D12, E12, F12 inhibitor controls at 2 μM, 1 μM, and 0.4 μM respectively; wells G12 and H12 are without ATP and serve as background controls.

4. Screening Protocol

[0203]

- Wash plate 1 time with TBS Tween-20 buffer with 1 min soak time.
- Dispense 39 μl of assay buffer
- Add 5 μl of 10X biotin-Gastrin mixture to all wells,
- Add 1 μl of test compound
- Add 5 μl 10 HGFR (with/without inhibitor control in column 12)
- Incubate at room temperature for 11 minutes
- Stop reaction by washing plate 3 times with TBS Tween-20
- Add 50 μl of 1:5200 Anti-PY-Eu antibody in Ab diluent and incubate at room temperature for 35 hr.
- Wash plate 3 times with TBS Tween-20
- Add 50 μl enhancement solution and incubate at room temperature for 1 hr.
- Read plate at Ex: 340 nm and Em:615 nm in time-resolved fluorescence (TRF) mode.

5. Data Analysis

[0204] Percent inhibition for each well is calculated using the wells A12, B12 and C12 as enzyme controls and wells G12 and H12 as background controls.

While the invention has been described in terms of various preferred embodiments and specific examples, the invention should be understood as not being limited by the foregoing detailed description, but as being defined by the appended claims and their equivalents. Accordingly, those skilled in the art will recognize that various changes and modifications

can be made without departing from the spirit and scope of the invention. Thus, the invention should be understood as not being limited by the foregoing detailed description, but as being defined by the appended claims and their equivalents.

All U.S. and foreign patents, published patent applications, and other references cited herein are hereby incorporated by reference in their entireties.

SEQUENCE LISTING

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<120> Catalytic Domains Of The Human Hepatocyte Growth Factor Receptor Tyrosine Kinase, And Materials And Methods For Identification Of Inhibitors Thereof

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tgtttaagcc ttttgaaaag ccagtgatga tctcaatggg caatgaaaat gtactggaaa 2820

ttaagggaaa tgatattgac cctgaagcag ttaaaggtga agtgttaaaa gttggaaata 2880

agagctgtga gaatatacac ttacattctg aagccgtttt atgcacggtc cccaatgacc 2940

tgctgaaatt gaacagcgag ctaaatatag agtggaagca agcaatttct tcaaccgtcc 3000

ttggaaaagt aatagttcaa ccagatcaga atttcacagg attgattgct ggtgttgtct 3060

caatatcaac agcactgtta ttactacttg ggtttttcct gtggctgaaa aagagaaagc 3120

aaattaaaga tctgggcagt gaattagttc gctacgatgc aagagtacac actcctcatt 3180

tggataggct tgtaagtgcc cgaagtgtaa gcccaactac agaaatggtt tcaaatgaat 3240

ctgtagacta ccgagctact tttccagaag atcagtttcc taattcatct cagaacggtt 3300

catgccgaca agtgcagtat cctctgacag acatgtcccc catcctaact agtggggact 3360

ctgatatatc cagtccatta ctgcaaaata ctgtccacat tgacctcagt gctctaaatc 3420

cagagctggt ccaggcagtg cagcatgtag tgattgggcc cagtagcctg attgtgcatt 3480

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ttaccaccaa gtcagatgtg tggtcctttg gcgtcgtcct ctgggagctg atgacaagag 4080

gagccccacc ttatcctgac gtaaacacct ttgatataac tgtttacttg ttgcaaggga 4140

gaagactcct acaacccgaa tactgcccag accccttata tgaagtaatg ctaaaatgct 4200

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<212> PRT
<213> human HGFR

<400> 2

Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15

Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30

Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45

Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60

Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80

Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95

Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110

Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125

Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140

Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160

Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175

Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190

Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205

His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220

Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240

Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255

Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270

Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285

His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300

Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320

Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335

Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350

Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365

Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380

Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385 390 395 400

Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
405 410 415

Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
420 425 430

```
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
      435             440             445

Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
   450             455             460

Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465             470             475             480

Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
            485             490             495

Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
         500             505             510

Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
      515             520             525

Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
   530             535             540

Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545             550             555             560

Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
            565             570             575

Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
         580             585             590

Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
      595             600             605

Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
   610             615             620

Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625             630             635             640

Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
            645             650             655
```

```
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
        660             665             670

Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
     675             680             685

His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
   690             695             700

Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705             710             715             720

Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
            725             730             735

Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
        740             745             750

Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
     755             760             765

Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
   770             775             780

Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785             790             795             800

Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
            805             810             815

Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
        820             825             830

Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
     835             840             845

Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
   850             855             860

Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
865             870             875             880

Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
            885             890             895
```

```
Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Trp Lys
        900             905             910

Gln Ala Ile Ser Ser Thr Val Leu Gly Lys Val Ile Val Gln Pro Asp
     915             920             925

Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala
   930             935             940

Leu Leu Leu Leu Leu Gly Phe Phe Leu Trp Leu Lys Lys Arg Lys Gln
945             950             955             960

Ile Lys Asp Leu Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His
           965             970             975

Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr
        980             985             990

Thr Glu Met Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro
     995             1000            1005

Glu Asp Gln Phe Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln
   1010            1015            1020

Val Gln Tyr Pro Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly
   1025            1030            1035

Asp Ser Asp Ile Ser Ser Pro Leu Leu Gln Asn Thr Val His Ile
   1040            1045            1050

Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala Val Gln His
   1055            1060            1065

Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn Glu Val
   1070            1075            1080

Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu Leu
   1085            1090            1095

Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
   1100            1105            1110
```

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly
1115 1120 1125

Ile Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu
1130 1135 1140

Gly Ile Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro
1145 1150 1155

Tyr Met Lys His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr
1160 1165 1170

His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val
1175 1180 1185

Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe Val His Arg
1190 1195 1200

Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe Thr Val
1205 1210 1215

Lys Val Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys Glu
1220 1225 1230

Tyr Tyr Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys
1235 1240 1245

Trp Met Ala Leu Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys
1250 1255 1260

Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Leu Met Thr
1265 1270 1275

Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr
1280 1285 1290

Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu Tyr Cys
1295 1300 1305

Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His Pro Lys
1310 1315 1320

Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile Ser
1325 1330 1335

```
Ala Ile Phe Ser Thr Phe Ile Gly Glu His Tyr Val His Val Asn
  1340            1345            1350

Ala Thr Tyr Val Asn Val Lys Cys Val Ala Pro Tyr Pro Ser Leu
  1355            1360            1365

Leu Ser Ser Glu Asp Asn Ala Asp Asp Glu Val Asp Thr Arg Pro
  1370            1375            1380

Ala Ser Phe Trp Glu Thr Ser
  1385            1390
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<211> 298
<212> PRT
<213> human catalytic domain wild-type HGFR

<400> 3

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Val His Ile Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala Val
1           5              10              15

Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn Glu
        20              25              30

Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu Leu
    35              40              45

Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn Arg
  50              55              60

Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile Ile
65              70              75              80

Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile Cys
            85              90              95

Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys His
        100             105             110

Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr Val
    115             120             125

Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Gly Met Lys Tyr
```

130 135 140

Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn Cys
145 150 155 160

Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu Ala
165 170 175

Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr Gly
180 185 190

Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr Gln
195 200 205

Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp
210 215 220

Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe
225 230 235 240

Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu
245 250 255

Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His Pro
260 265 270

Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile Ser
275 280 285

Ala Ile Phe Ser Thr Phe Ile Gly Glu His
290 295

<210> 4
<211> 299
<212> PRT
<213> human catalytic domain wild-type HGFR

<400> 4

Met Val His Ile Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala
1 5 10 15

Val Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn
20 25 30

```
Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu
     35            40            45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
   50            55            60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65            70            75            80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
          85            90            95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
        100           105           110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
     115           120           125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys
   130           135           140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145           150           155           160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
          165           170           175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
        180           185           190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
     195           200           205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
   210           215           220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225           230           235           240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
          245           250           255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
        260           265           270
```

```
Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
     275             280             285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
  290             295


<210> 5
<211> 299
<212> PRT
<213> human catalytic domain wild-type HGFR

<400> 5

Met Val His Ile Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala
1               5               10              15

Val Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn
            20              25              30

Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu
        35              40              45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
    50              55              60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65              70              75              80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
                85              90              95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
            100             105             110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
        115             120             125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Gly Met Lys
    130             135             140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145             150             155             160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
```

165 170 175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
180 185 190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
195 200 205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210 215 220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225 230 235 240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
245 250 255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
260 265 270

Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
275 280 285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
290 295

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<213> synthetic nucleotide primer

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<210> 7
<211> 40
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<400> 7
ctagaagctt ctagtgctcc ccaatgaaag tagagaagat 40

<210> 8
<211> 15
<212> PRT
<213> synthetic peptide

<400> 8

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys
1 5 10 15

<210> 9
<211> 299
<212> PRT
<213> HGFR M1250T Kinase

<400> 9

Met Val His Ile Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala
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Val Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn
20 25 30

Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu
35 40 45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
50 55 60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65 70 75 80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
85 90 95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
100 105 110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
115 120 125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys
130 135 140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145 150 155 160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
165 170 175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr

180 185 190

Gly Ala Lys Leu Pro Val Lys Trp Thr Ala Leu Glu Ser Leu Gln Thr
195 200 205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210 215 220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225 230 235 240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
245 250 255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
260 265 270

Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
275 280 285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
290 295

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<211> 897
<212> DNA
<213> HGFR Y 1230C

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ggttgtgtat atcatgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg 180

aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc 240

atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt 300

gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt 360

cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc 420

aaagggatga aatatcttgc aagcaaaaag tttgtccaca gagacttggc tgcaagaaac 480

tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg 540

tgtgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg 600

atggctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt 660

ggcgtcgtcc tctgggagct gatgacaaga ggagccccac cttatcctga cgtaaacacc 720

tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca 780

gaccccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc 840

ttttctgaac tggtgtcccg gatatcagcg atcttctcta ctttcattgg ggagcac 897

<210> 11
<211> 897
<212> DNA
<213> HGFR M1250T

<400> 11
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gtgattgggc ccagtagcct gattgtgcat ttcaatgaag tcataggaag agggcatttt 120

ggttgtgtat atcatgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg 180

aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc 240

atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt 300

gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt 360

cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc 420

aaaggcatga aatatcttgc gagcaaaaag tttgtccaca gagacttggc tgcaagaaac 480

tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg 540

tatgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg 600

accgctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt 660

ggcgtgctcc tctgggagct gatgacaaga ggagccccac cttatcctga tgtaaacacc 720

tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca 780

gaccccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc 840

ttttctgaac tggtgtcccg gatatcagcg atcttctcta ctttcattgg ggagcac 897

<210> 12
<211> 1281
<212> DNA
<213> Human HGFR intracellular domain

<400> 12
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gtaagtgccc gaagtgtaag cccaactaca gaaatggttt caaatgaatc tgtagactac 120

cgagctactt ttccagaaga tcagtttcct aattcatctc agaacggttc atgccgacaa 180

gtgcagtatc ctctgacaga catgtccccc atcctaacta gtggggactc tgatatatcc 240

agtccattac tgcaaaatac tgtccacatt gacctcagtg ctctaaatcc agagctggtc 300

caggcagtgc agcatgtagt gattgggccc agtagcctga ttgtgcattt caatgaagtc 360

ataggaagag ggcattttgg ttgtgtatat catgggactt tgttggacaa tgatggcaag 420

aaaattcact gtgctgtgaa atccttgaac agaatcactg acataggaga agtttcccaa 480

tttctggccg agggaatcat catgaaagat tttagtcatc ccaatgtcct ctcgctcctg 540

ggaatctgcc tgcgaagtga agggtctccg ctggtggtcc taccatacat gaaacatgga 600

gatcttcgaa atttcattcg aaatgagact cataatccaa ctgtaaaaga tcttattggc 660

tttggtcttc aagtagccaa aggcatgaaa tatcttgcaa gcaaaaagtt tgtccacaga 720

gacttggctg caagaaactg tatgctggat gaaaaattca cagtcaaggt tgctgatttt 780

ggtcttgcca gagacatgta tgataaagaa tactatagtg tacacaacaa aacaggtgca 840

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Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro Glu Asp Gln
35 40 45

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Phe Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln Val Gln Tyr Pro
  50            55            60

Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly Asp Ser Asp Ile Ser
65            70            75            80

Ser Pro Leu Leu Gln Asn Thr Val His Ile Asp Leu Ser Ala Leu Asn
          85            90            95

Pro Glu Leu Val Gln Ala Val Gln His Val Val Ile Gly Pro Ser Ser
       100           105           110

Leu Ile Val His Phe Asn Glu Val Ile Gly Arg Gly His Phe Gly Cys
     115           120           125

Val Tyr His Gly Thr Leu Leu Asp Asn Asp Gly Lys Lys Ile His Cys
  130           135           140

Ala Val Lys Ser Leu Asn Arg Ile Thr Asp Ile Gly Glu Val Ser Gln
145           150           155           160

Phe Leu Ala Glu Gly Ile Ile Met Lys Asp Phe Ser His Pro Asn Val
          165           170           175

Leu Ser Leu Leu Gly Ile Cys Leu Arg Ser Glu Gly Ser Pro Leu Val
       180           185           190

Val Leu Pro Tyr Met Lys His Gly Asp Leu Arg Asn Phe Ile Arg Asn
     195           200           205

Glu Thr His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe Gly Leu Gln
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Val Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe Val His Arg
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Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe Thr Val Lys
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Val Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr
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Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys Trp Met Ala
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Ser Phe Gly Val Leu Leu Trp Glu Leu Met Thr Arg Gly Ala Pro Pro
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Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly
325 330 335

Arg Arg Leu Leu Gln Pro Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val
340 345 350

Met Leu Lys Cys Trp His Pro Lys Ala Glu Met Arg Pro Ser Phe Ser
355 360 365

Glu Leu Val Ser Arg Ile Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu
370 375 380

His Tyr Val His Val Asn Ala Thr Tyr Val Asn Val Lys Cys Val Ala
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Asp Thr Arg Pro Ala Ser Phe Trp Glu Thr Ser
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20 25 30

Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr Arg Gly Thr Leu
35 40 45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
50 55 60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65 70 75 80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
85 90 95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
100 105 110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
115 120 125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys

130 135 140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145 150 155 160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
165 170 175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
180 185 190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
195 200 205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210 215 220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225 230 235 240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
245 250 255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
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Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
275 280 285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
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Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu
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Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
  50              55              60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65              70              75              80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
            85              90              95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
        100             105             110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
    115             120             125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys
130             135             140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
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Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
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Ala Arg Asp Met Cys Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
        180             185             190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
    195             200             205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210             215             220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225             230             235             240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
            245             250             255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
        260             265             270
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Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
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Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
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Annex to the application documents - subsequently filed sequences listing

[0205]

SEQUENCE LISTING

<110> Agouron, Pharmaceuticals, Inc.

<120> Catalytic Domains Of The Human Hepatocyte Growth Factor Receptor Tyrosine Kinase, And Materials And Methods For Identification Of Inhibitors Thereof

<130> 0128-US

<140> 02.006616.3
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35 40 45

Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60

Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80

Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95

Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110

Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125

Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140

Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160

Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175

Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190

Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205

His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220

Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240

Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255

Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270

Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285

His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300

Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320

Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335

Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350

Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
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Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380

Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
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Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
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Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
420 425 430

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Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465             470             475             480

Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485             490             495

Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500             505             510

Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515             520             525

Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530             535             540

Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545             550             555             560

Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565             570             575

Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580             585             590

Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595             600             605

Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610             615             620

Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625             630             635             640

Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645             650             655
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Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
        660             665             670

Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
     675             680             685

His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
   690             695             700

Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705             710             715             720

Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
            725             730             735

Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
        740             745             750

Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
      755             760             765

Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
   770             775             780

Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785             790             795             800

Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
            805             810             815

Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
        820             825             830

Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
      835             840             845

Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
   850             855             860

Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
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Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
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Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala
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945             950             955             960

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            965             970             975

Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr
        980             985             990

Thr Glu Met Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro
      995             1000            1005

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   1010            1015            1020

Val Gln Tyr Pro Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly
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Asp Ser Asp Ile Ser Ser Pro Leu Leu Gln Asn Thr Val His Ile
   1040            1045            1050

Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala Val Gln His
   1055            1060            1065

Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn Glu Val
   1070            1075            1080

Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu Leu
   1085            1090            1095

Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
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Tyr Met Lys His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr
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His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val
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Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe Val His Arg
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Lys Val Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys Glu
1220 1225 1230

Tyr Tyr Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys
1235 1240 1245

Trp Met Ala Leu Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys
1250 1255 1260

Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Leu Met Thr
1265 1270 1275

Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr
1280 1285 1290

Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu Tyr Cys
1295 1300 1305

Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His Pro Lys
1310 1315 1320

Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile Ser
1325 1330 1335

Ala Ile Phe Ser Thr Phe Ile Gly Glu His Tyr Val His Val Asn
1340 1345 1350

Ala Thr Tyr Val Asn Val Lys Cys Val Ala Pro Tyr Pro Ser Leu
1355 1360 1365

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Ala Ser Phe Trp Glu Thr Ser
1385 1390

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Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn Glu
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Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu Leu
35 40 45

Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn Arg
50 55 60

Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile Ile
65 70 75 80

Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile Cys
85 90 95

Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys His
100 105 110

Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr Val
115 120 125

Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Gly Met Lys Tyr

130 135 140

Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn Cys
145 150 155 160

Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu Ala
165 170 175

Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr Gly
180 185 190

Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr Gln
195 200 205

Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp
210 215 220

Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe
225 230 235 240

Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu
245 250 255

Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His Pro
260 265 270

Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile Ser
275 280 285

Ala Ile Phe Ser Thr Phe Ile Gly Glu His
290 295

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<400> 4

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1 5 10 15

Val Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn
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Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu
     35            40            45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
  50            55            60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65            70            75            80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
           85            90            95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
       100           105           110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
     115           120           125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys
  130           135           140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145           150           155           160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
           165           170           175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
       180           185           190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
     195           200           205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
  210           215           220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225           230           235           240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
           245           250           255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
       260           265           270
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<400> 5

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35 40 45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
50 55 60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65 70 75 80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
85 90 95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
100 105 110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
115 120 125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Gly Met Lys
130 135 140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145 150 155 160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu

165 170 175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
180 185 190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
195 200 205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210 215 220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225 230 235 240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
245 250 255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
260 265 270

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275 280 285

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290 295

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<210> 8
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<400> 8

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<210> 9
<211> 299
<212> PRT
<213> HGFR M1250T Kinase

<400> 9

Met Val His Ile Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala
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Val Gln His Val Val Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn
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35 40 45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
50 55 60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65 70 75 80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
85 90 95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
100 105 110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
115 120 125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys
130 135 140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145 150 155 160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
165 170 175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr

180 185 190

Gly Ala Lys Leu Pro Val Lys Trp Thr Ala Leu Glu Ser Leu Gln Thr
195 200 205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210 215 220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225 230 235 240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
245 250 255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
260 265 270

Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
275 280 285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
290 295

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<211> 897
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ggttgtgtat atcatgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg 180

aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc 240

atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt 300

gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt 360

cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc 420

aaagggatga aatatcttgc aagcaaaaag tttgtccaca gagacttggc tgcaagaaac 480

tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg 540

tgtgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg 600

atggctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt 660

ggcgtcgtcc tctgggagct gatgacaaga ggagccccac cttatcctga cgtaaacacc 720

tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca 780

gacccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc 840

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ggttgtgtat atcatgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg 180

aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc 240

atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt 300

gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt 360

cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc 420

aaaggcatga aatatcttgc gagcaaaaag tttgtccaca gagacttggc tgcaagaaac 480

tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg 540

tatgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg 600

accgctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt 660

ggcgtgctcc tctgggagct gatgacaaga ggagccccac cttatcctga tgtaaacacc 720

tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca 780

gacccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc 840

ttttctgaac tggtgtcccg gatatcagcg atcttctcta ctttcattgg ggagcac 897

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cgagctactt ttccagaaga tcagtttcct aattcatctc agaacggttc atgccgacaa 180

gtgcagtatc ctctgacaga catgtccccc atcctaacta gtggggactc tgatatatcc 240

agtccattac tgcaaaatac tgtccacatt gacctcagtg ctctaaatcc agagctggtc 300

caggcagtgc agcatgtagt gattgggccc agtagcctga ttgtgcattt caatgaagtc 360

ataggaagag ggcattttgg ttgtgtatat catgggactt tgttggacaa tgatggcaag 420

aaaattcact gtgctgtgaa atccttgaac agaatcactg acataggaga agtttcccaa 480

tttctggccg agggaatcat catgaaagat tttagtcatc ccaatgtcct ctcgctcctg 540

ggaatctgcc tgcgaagtga agggtctccg ctggtggtcc taccatacat gaaacatgga 600

gatcttcgaa atttcattcg aaatgagact cataatccaa ctgtaaaaga tcttattggc 660

tttggtcttc aagtagccaa aggcatgaaa tatcttgcaa gcaaaaagtt tgtccacaga 720

gacttggctg caagaaactg tatgctggat gaaaaattca cagtcaaggt tgctgatttt 780

ggtcttgcca gagacatgta tgataaagaa tactatagtg tacacaacaa aacaggtgca 840

aagctgccag tgaagtggat ggctttggaa agtctgcaaa ctcaaaagtt taccaccaag 900

tcagatgtgt ggtcctttgg cgtgctcctc tgggagctga tgacaagagg agccccacct 960

tatcctgatg taaacacctt tgatataact gtttacttgt tgcaagggag aagactccta 1020

caacccgaat actgcccaga ccccttatat gaagtaatgc taaaatgctg gcaccctaaa 1080

gccgaaatgc gcccatcctt ttctgaactg gtgtcccgga tatcagcaat cttctctact 1140

ttcattgggg agcactatgt ccatgtgaac gctacttatg tgaacgtaaa atgtgtcgct 1200

ccatatccat ctctgttgtc atcagaagat aacgctgatg atgaggtgga cacacgacca 1260

gcctccttct gggagacatc a 1281

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<400> 13

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Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro Glu Asp Gln
35 40 45

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Phe Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln Val Gln Tyr Pro
  50            55            60

Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly Asp Ser Asp Ile Ser
65            70            75            80

Ser Pro Leu Leu Gln Asn Thr Val His Ile Asp Leu Ser Ala Leu Asn
            85            90            95

Pro Glu Leu Val Gln Ala Val Gln His Val Val Ile Gly Pro Ser Ser
        100           105           110

Leu Ile Val His Phe Asn Glu Val Ile Gly Arg Gly His Phe Gly Cys
    115           120           125

Val Tyr His Gly Thr Leu Leu Asp Asn Asp Gly Lys Lys Ile His Cys
130           135           140

Ala Val Lys Ser Leu Asn Arg Ile Thr Asp Ile Gly Glu Val Ser Gln
145           150           155           160

Phe Leu Ala Glu Gly Ile Ile Met Lys Asp Phe Ser His Pro Asn Val
            165           170           175

Leu Ser Leu Leu Gly Ile Cys Leu Arg Ser Glu Gly Ser Pro Leu Val
        180           185           190

Val Leu Pro Tyr Met Lys His Gly Asp Leu Arg Asn Phe Ile Arg Asn
    195           200           205

Glu Thr His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe Gly Leu Gln
210           215           220

Val Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe Val His Arg
225           230           235           240

Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe Thr Val Lys
            245           250           255

Val Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr
        260           265           270

Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys Trp Met Ala
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275 280 285

Leu Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys Ser Asp Val Trp
290 295 300

Ser Phe Gly Val Leu Leu Trp Glu Leu Met Thr Arg Gly Ala Pro Pro
305 310 315 320

Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly
325 330 335

Arg Arg Leu Leu Gln Pro Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val
340 345 350

Met Leu Lys Cys Trp His Pro Lys Ala Glu Met Arg Pro Ser Phe Ser
355 360 365

Glu Leu Val Ser Arg Ile Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu
370 375 380

His Tyr Val His Val Asn Ala Thr Tyr Val Asn Val Lys Cys Val Ala
385 390 395 400

Pro Tyr Pro Ser Leu Leu Ser Ser Glu Asp Asn Ala Asp Asp Glu Val
405 410 415

Asp Thr Arg Pro Ala Ser Phe Trp Glu Thr Ser
420 425

<210> 14
<211> 897
<212> DNA
<213> HGFR H1094R DNA

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ggttgtgtat atcgtgggac tttgttggac aatgatggca agaaaattca ctgtgctgtg 180

aaatccttga acagaatcac tgacatagga gaagtttccc aatttctgac cgagggaatc 240

atcatgaaag attttagtca tcccaatgtc ctctcgctcc tgggaatctg cctgcgaagt 300

gaagggtctc cgctggtggt cctaccatac atgaaacatg gagatcttcg aaatttcatt 360

cgaaatgaga ctcataatcc aactgtaaaa gatcttattg gctttggtct tcaagtagcc 420

aaagggatga aatatcttgc aagcaaaaag tttgtccaca gagacttggc tgcaagaaac 480

tgtatgctgg atgaaaaatt cacagtcaag gttgctgatt ttggtcttgc cagagacatg 540

tatgataaag aatactatag tgtacacaac aaaacaggtg caaagctgcc agtgaagtgg 600

atggctttgg aaagtctgca aactcaaaag tttaccacca agtcagatgt gtggtccttt 660

ggcgtcgtcc tctgggagct gatgacaaga ggagccccac cttatcctga cgtaaacacc 720

tttgatataa ctgtttactt gttgcaaggg agaagactcc tacaacccga atactgccca 780

gacccttat atgaagtaat gctaaaatgc tggcacccta aagccgaaat gcgcccatcc 840

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<211> 299
<212> PRT
<213> HGFR H1094R Kinase

<400> 15

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20 25 30

Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr Arg Gly Thr Leu
35 40 45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
50 55 60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65 70 75 80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
85 90 95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
100 105 110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
115 120 125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys

130 135 140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145 150 155 160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
165 170 175

Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
180 185 190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
195 200 205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210 215 220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225 230 235 240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
245 250 255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
260 265 270

Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
275 280 285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
290 295

<210> 16
<211> 299
<212> PRT
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<400> 16

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20 25 30

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Glu Val Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu
  35            40            45

Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn
  50            55            60

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly Ile
65            70            75            80

Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu Gly Ile
            85            90            95

Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro Tyr Met Lys
        100           105           110

His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr His Asn Pro Thr
    115           120           125

Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val Ala Lys Ala Met Lys
130           135           140

Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145           150           155           160

Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val Ala Asp Phe Gly Leu
            165           170           175

Ala Arg Asp Met Cys Asp Lys Glu Tyr Tyr Ser Val His Asn Lys Thr
        180           185           190

Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr
    195           200           205

Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu
210           215           220

Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr
225           230           235           240

Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro
            245           250           255

Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His
        260           265           270
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Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile
 275                 280                 285

Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
 290                 295
```

Claims

1. An isolated polynucleotide which encodes the human hepatocyte growth factor receptor or the human hepatocyte gowth factor receptor kinase domain, or a fragment or variant thereof.

2. An isolated polynucleotide according to claim 1, wherein the nucleotide sequence of said polynucleotide corresponds to at least bases 3342 to 4206 of SEQ ID NO: 1.

3. An isolated polynucleotide according to claim 1, wherein the nucleotide sequence of said polynucleotide corresponds to the sequence of SEQ ID NO: 10.

4. An isolated polynucleotide according to claim 1, wherein the nucleotide sequence of said polynucleotide corresponds to the sequence of SEQ ID NO: 11.

5. An isolated polynucleotide according to claim 1, wherein the nucleotide sequence of said polynucleotide corresponds to the sequence of SEQ ID NO: 12.

6. An isolated polynucleotide according to claim 1, wherein the nucleotide sequence of said polynucleotide corresponds to the sequence of SEQ ID NO: 14.

7. A crystal structure comprising the human hepatocyte growth factor receptor kinase.

8. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase corresponds to at least amino acids 1051 to 1348 of SEQ ID NO: 2.

9. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase corresponds to the sequence of SEQ ID NO: 3.

10. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase corresponds to the sequence of SEQ ID NO: 4.

11. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase corresponds to the sequence of SEQ ID NO: 5.

12. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence of SEQ ID NO: 6.

13. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence of SEQ ID NO: 7.

14. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence of SEQ ID NO: 8.

15. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence

of SEQ ID NO: 9.

16. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence of SEQ ID NO: 13.

17. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence of SEQ ID NO: 15.

18. A crystal structure according to claim 7 wherein the amino acid sequence of said kinase comprises the sequence of SEQ ID NO: 16.

19. An isolated polypeptide comprising the human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain, or a variant thereof.

20. A polypeptide according to claim 19 wherein said human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain comprises a deletion that imparts favorable physical characteristics to the resulting polypeptide.

21. A polypeptide according to claim 19 wherein said polypeptide comprises amino acids 1051 to 1341 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

22. A polypeptide according to claim 19 wherein said polypeptide comprises amino acids 1051 to 1348 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

23. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 3 or a conservatively substituted variant thereof.

24. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 4 or a conservatively substituted variant thereof.

25. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 5 or a conservatively substituted variant thereof.

26. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 6 or a conservatively substituted variant thereof.

27. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 7 or a conservatively substituted variant thereof.

28. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 8 or a conservatively substituted variant thereof.

29. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 9 or a conservatively substituted variant thereof.

30. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 13 or a conservatively substituted variant thereof.

31. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 15 or a conservatively substituted variant thereof.

32. A polypeptide according to claim 19 wherein said polypeptide comprises the amino acid sequence as set forth in SEQ ID NO. 16 or a conservatively substituted variant thereof.

33. An isolated polynucleotide which encodes the catalytically active form of the human hepatocyte growth factor receptor or human hepatocyte growth factor receptor kinase domain, or a fragment or variant thereof.

34. An isolated catalytically active polypeptide comprising the human hepatocyte growth factor receptor or human

hepatocyte growth factor receptor kinase domain, or a variant thereof.

35. An isolated polynucleotide which encodes the catalytic domain of the human hepatocyte growth factor receptor kinase, or a fragment or variant thereof.

36. An isolated catalytically active polypeptide comprising the catalytic domain of the human hepatocyte growth factor receptor kinase or a variant thereof.

37. An isolated soluble polypeptide comprising the catalytic domain of the human hepatocyte growth factor receptor kinase or a variant thereof.

38. An expression vector for producing the human hepatocyte growth factor receptor kinase in a host cell, which vector comprises: a polynucleotide encoding the human hepatocyte growth factor receptor kinase or a variant thereof; and regulatory sequences functional in said host cell operably linked to said polynucleotide.

39. A vector according to claim 38 wherein said polynucleotide encodes the active human hepatocyte growth factor receptor kinase, said active kinase comprising bases 3342 to 4206 of SEQ ID NO: 1.

40. A vector according to claim 38 wherein said vector is selected from the group consisting of pET28a, pAcSG2, and pFastBac.

41. A vector according to claim 38 wherein said vector is pFastBac-NcoI.

42. A vector according to claim 38 wherein said host cell is *E. coli.*

43. A host cell transformed or transfected with a polynucleotide encoding the human hepatocyte growth factor receptor kinase or a variant thereof.

44. A host cell according to claim 43 wherein said host cell is transformed or transfected with said polynucleotide via an expression vector comprising said polynucleotide; a regulatory sequence functional in said host cell operably linked to said polynucleotide; and a selectable marker.

45. A host cell according to claim 44 wherein said expression vector is selected from the group consisting of: pET28a, pAcSG2, and pFastBac.

46. A host cell according to claim 44 wherein said expression vector is pFastBac-*Nco*I.

47. A host cell according to claim 43 wherein said polynucleotide encodes the human hepatocyte growth factor receptor kinase, said kinase comprising bases 3342 to 4206 of SEQ ID NO: 1.

48. A host cell according to claim 43 wherein said host is *E. coli.*

49. A host cell according to claim 43 wherein said host is infected with a recombinant baculovirus.

50. A host cell according to claim 43 wherein said host is an insect cell.

51. A host cell according to claim 50 wherein said insect cell is Sf9.

52. A method of producing a polypeptide or variant thereof comprising culturing the host cell of claim 43 under conditions such that said polypeptide or variant thereof is expressed, and recovering said polypeptide or variant thereof.

53. A method for assaying a candidate compound for its ability to interact with the human hepatocyte growth factor receptor comprising:

(a) expressing an isolated DNA sequence or variant thereof encoding at least the kinase domain of said human hepatocyte growth factor receptor in a host capable of producing said kinase, said kinase being in a form which may be assayed for interaction of said kinase with said candidate compound;
(b) exposing said kinase to said candidate compound; and

(c) evaluating the interaction of said kinase with said candidate compound.

54. A method according to claim 53 wherein said evaluation step comprises:

(a) crystallizing said kinase in a condition suitable for x-ray crystallography; and
(b) conducting x-ray crystallography on said kinase.

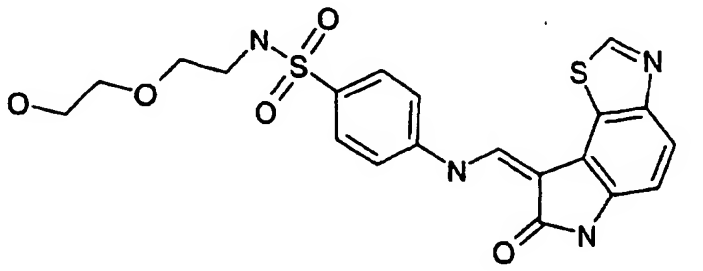
55. A method according to claim 53 wherein the results of said x-ray crystallography step (b) are used to determine the three dimensional molecular structure of the configuration of human hepatocyte growth factor receptor kinase and the binding pockets thereof.

56. A crystal structure comprising a polypeptide encoded by a polynucleotide which encodes at least the human hepatocyte growth factor receptor kinase domain, or a fragment or variant thereof.

57. A crystal structure comprising a polypeptide encoded by a polynucleotide which encodes at least the human hepatocyte growth factor receptor kinase domain, or a fragment or variant thereof, and a ligand complexed thereto.

58. A crystal structure according to claim 57 wherein said ligand modulates the activity of human hepatocyte growth factor kinase.

59. A crystal structure according to claim 58 wherein said ligand is a compound of the formula:



60. A process of drug design for compounds which interact with the human hepatocyte growth factor receptor kinase comprising:

(a) crystallizing said human hepatocyte growth factor receptor kinase;
(b) resolving the x-ray crystallography of said kinase;
(c) applying the data generated from resolving the x-ray crystallography of said kinase to a computer algorithm which generates a model of said kinase suitable for use in designing molecules that will act as agonists or antagonists to said polypeptide; and
(d) applying an interative process whereby various molecular structures are applied to said computer-generated model to identify potential agonists or antagonists of said kinase.

61. A process according to claim 60 wherein said process is utilized to identify modulators of said active kinase, said modulators serving as lead compounds for the design of potentially therapeutic compounds for the treatment of diseases or disorders associated with the hepatocyte growth factor receptor- hepatocyte growth factor signaling pathway.

62. A method of rapidly screening large compound libraries to identify compounds that inhibit human hepatocyte growth factor receptor kinase comprising a non-radioactive immunosorbent assay capable of robotic control.

63. A method according to claim 62 wherein said assay is DELFIA.

64. A method of assessing compounds which are agonists or antagonists of the activity of the hepatocyte growth factor receptor kinase comprising:

(a) crystallizing said hepatocyte growth factor receptor kinase;
(b) obtaining crystallography coordinates for said crystallized hepatocyte growth factor receptor kinase;
(c) applying said crystallography coordinates for said hepatocyte growth factor receptor kinase to a computer algorithm such that said algorithm generates a model of said hepatocyte growth factor receptor kinase, said model suitable for use in designing molecules that will act as agonists or antagonists to said kinase; and
(d) applying an iterative process whereby various molecular structures are applied to said computer-generated model to identify potential agonists or antagonists to said kinase.

65. A method according to claim 64 further comprising the steps of:

(c) synthesizing or obtaining said agonist or antagonist; and
(d) contacting said agonist or antagonist with said molecule to determine the ability of said potential agonist or antagonist to interact with said molecule.

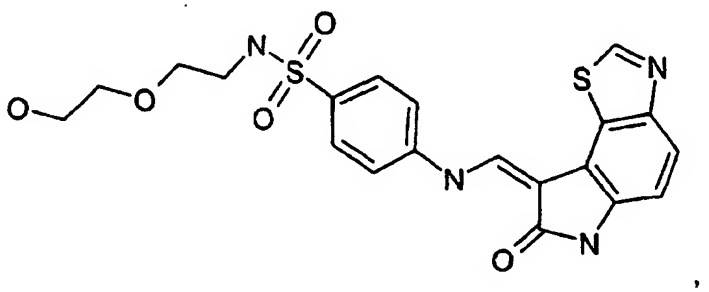
66. A method according to claim 64, wherein the crystallography coordinates comprise coordinates of hepatocyte growth factor receptor kinase amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231 which are within about a root mean square deviation of not more than about 1.5 Å from the backbone atoms of said amino acids according to Table 1.

67. A method according to claim 64, wherein the crystallography coordinates comprise coordinates of all the amino acids of hepatocyte growth factor receptor kinase which are within about a root mean square deviation of not more than about 1.5 Å from the backbone atoms of said amino acids according to Table 1.

68. A method for determining the three-dimensional structure of a complex of hepatocyte growth factor receptor kinase with a ligand thereof, comprising:

(a) obtaining x-ray diffraction data for crystals of the complex, and
(b) utilizing a set of atomic coordinates of Table 1 or portions thereof; and coordinates having a root mean square deviation therefrom with respect to conserved protein backbone atoms of not more than about 1.5 Å to define the three-dimensional structure of the complex.

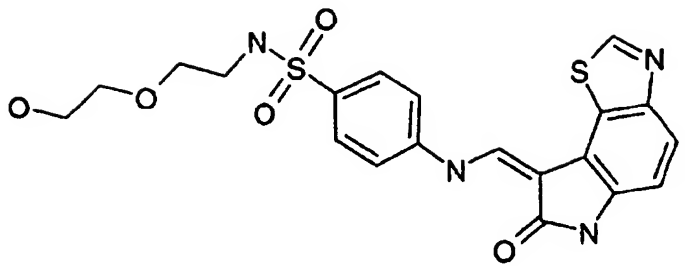
69. A method of using a three-dimensional structure of a polypeptide encoded by a polynucleotide which encodes the human hepatocyte growth factor receptor and a compound of the formula:



as defined by the structure coordinates of Table 1, or a portion thereof, in a drug-discovery strategy comprising:

(a) selecting a potential drug by performing rational drug design with the three-dimensional structure determined from one or more sets of atomic coordinates in Table 1, wherein said selecting is performed in conjunction with computer modeling;
(b) contacting the potential drug with a polypeptide containing a functional human hepatocyte growth factor receptor; and
(c) determining the binding of the potential drug with said polypeptide.

70. A method of using a three-dimensional structure of a polypeptide encoded by a polynucleotide which encodes the human hepatocyte growth factor receptor kinase domain and a compound of the formula:



as defined by the structure coordinates of Table 1, or a portion thereof, in a drug-discovery strategy comprising:

(a) selecting a potential drug by performing rational drug design with the three-dimensional structure determined from one or more sets of atomic coordinates in Table 1, wherein said selecting is performed in conjunction with computer modeling;
(b) contacting the potential drug with a polypeptide containing a functional human hepatocyte growth factor receptor; and
(c) determining if the potential drug modulates the activity of the polypeptide.

71. A method for evaluating the potential of a chemical entity to associate with:

(a) a molecule or molecular complex comprising a binding pocket defined by structure coordinates of human hepatocyte growth factor receptor amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231, according to Table 1, or

(b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than about 1.5 Å comprising the steps of:

(i) employing computational means to perform a fitting operation between the chemical entity and a binding pocket defined by structure coordinates of hepatocyte growth factor receptor amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231 which are within about a root mean square deviation of not more than about 1.5 Å from the backbone atoms of said amino acids according to Table 1; and

(ii) analyzing the results of said fitting operation to quantify the association between the chemical entity and the binding pocket.

72. A method according to claim 71, wherein said method evaluates the potential of a chemical entity to associate with a molecule or molecular complex:

(a) defined by structure coordinates of all of the hepatocyte growth factor receptor amino acids, as set forth in Table 1, or

(b) a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than about 1.5 Å

73. A computer for producing a three-dimensional representation of:

(a) a molecule or molecular complex, wherein said molecule or molecular complex comprises a binding pocket defined by the structure coordinates of hepatocyte growth factor receptor kinase amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231, according to Table 1; or

(b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than about

1.5 Å,

wherein said computer comprises:

(i) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises the structure coordinates of hepatocyte growth factor kinase amino acids 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231, according to Table 1;

(ii) a working memory for storing instructions for processing said computer-readable data;

(iii) a central-processing unit coupled to said working memory and to said computer-readable data storage medium for processing said computer-machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

74. A computer according to claim 73, wherein said computer produces a three-dimensional representation of:

(a) a molecule or molecular complex defined by structure coordinates of all of the hepatocyte growth factor kinase amino acids set forth in Table 1, or

(b) a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å; and

wherein said computer readable data contains the coordinates of all of the hepatocyte growth factor kinase amino acids set forth in Table 1.

75. A computer for determining at least a portion of the structure coordinates corresponding to the x-ray diffraction data obtained from a molecule or molecular complex, wherein said computer comprises:

(a) a computer-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises at least a portion of the structural coordinates of hepatocyte growth factor receptor kinase according to Table 1;

(b) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises x-ray diffraction data obtained from said molecule or molecular complex;

(c) a working memory for storing instructions for processing said computer-readable data of

(a) and (b);

(d) a central-processing unit coupled to said working memory and to said computer-readable data storage medium of (a) and (b) for performing a Fourier transform of the machine readable data of (a) and for processing said computer-readable data of (b) into structure coordinates; and

(e) a display coupled to said central-processing unit for displaying said structure coordinates of said molecule or molecular complex.

76. A computer readable medium having stored thereon data of the structure coordinates of a *Met* ligand-binding site comprising 1082-1086, 1091-1094, 1107-1110, 1140-1142, 1155-1175, 1208-1213, and 1219-1231 according to Table 1.

Figure 1

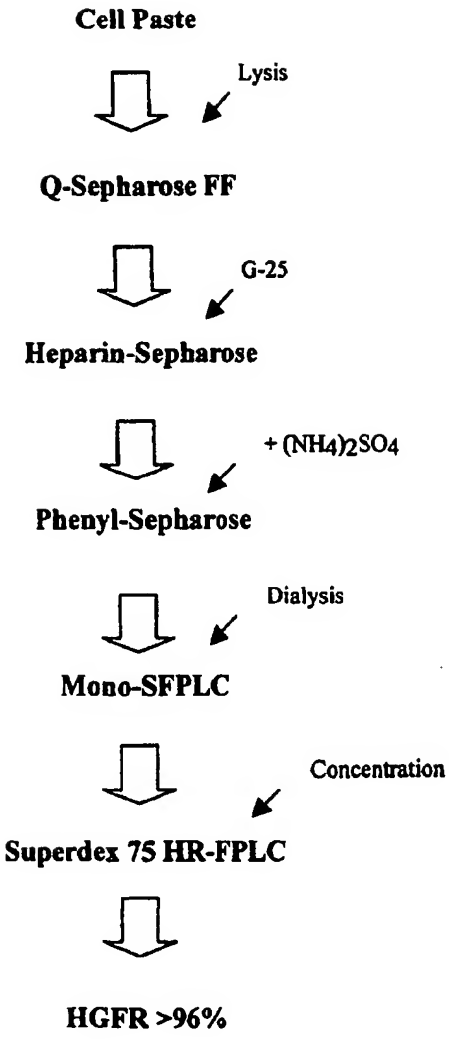

Cell Paste
Lysis
Q-Sepharose FF
G-25
Heparin-Sepharose
+ (NH4)2SO4
Phenyl-Sepharose
Dialysis
Mono-SFPLC
Concentration
Superdex 75 HR-FPLC
HGFR >96%

Figure 2

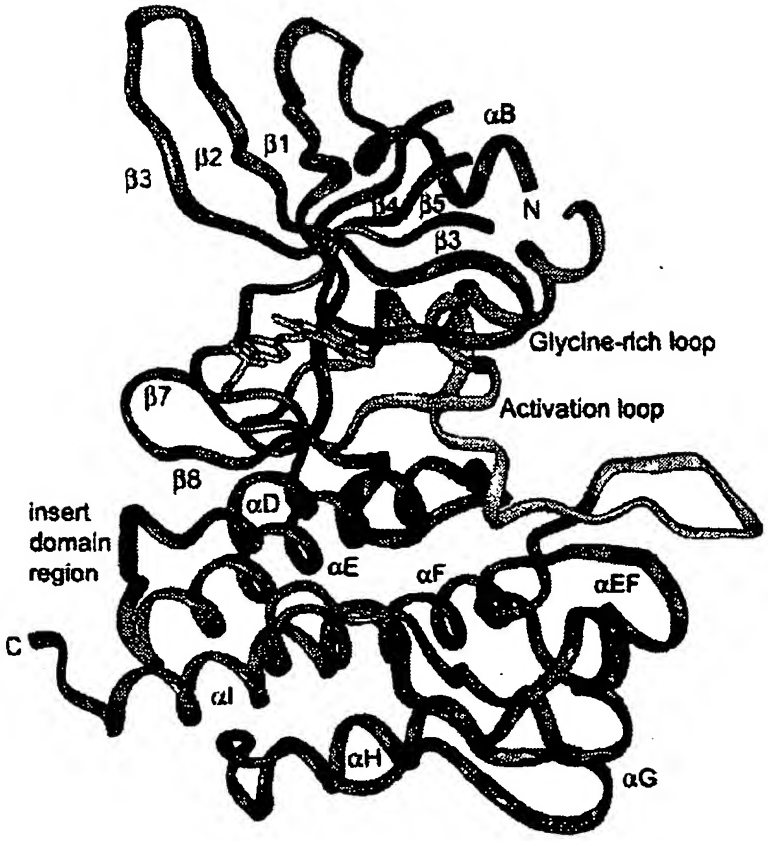

αB
β1
β2
β3
β4
β5
N
β3
Glycine-rich loop
Activation loop
β7
β8
αD
insert
domain
region
αE
αF
αEF
C
αI
αH
αG

Figure 3

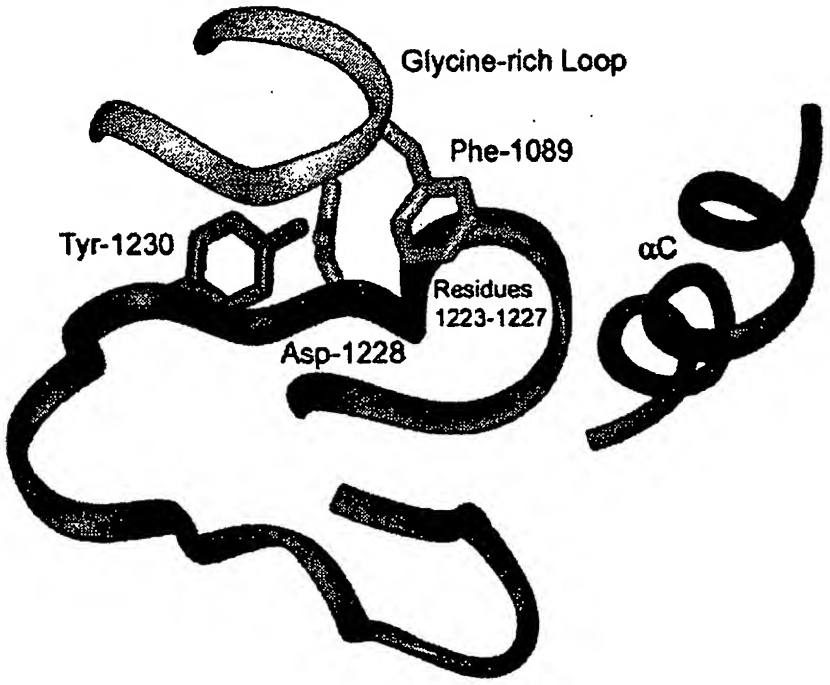

Glycine-rich Loop
Phe-1089
Tyr-1230
αC
Residues
1223-1227
Asp-1228

Figure 4

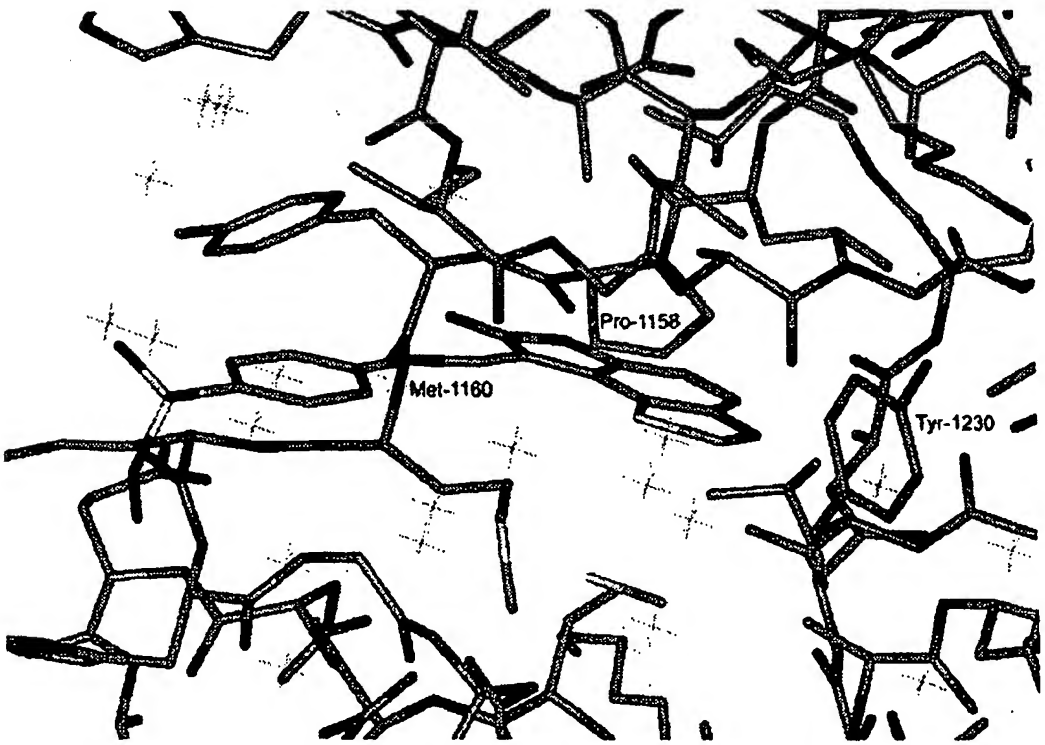


Figure 5(A)

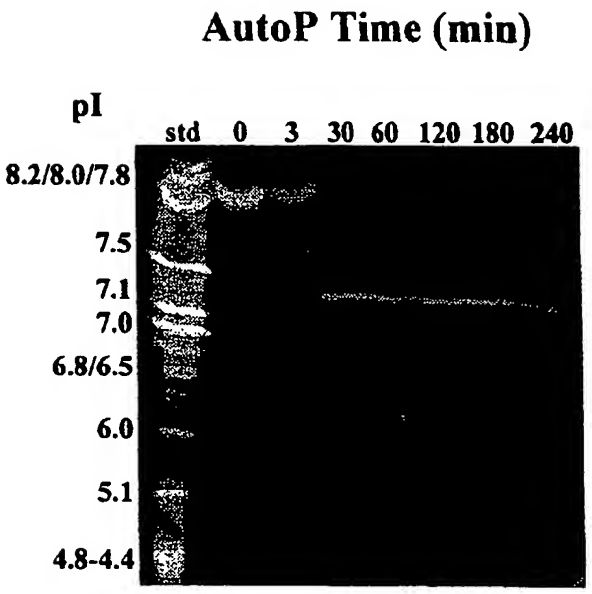

AutoP Time (min)
pI
std
0
3
30
60
120
180
240
8.2/8.0/7.8
7.5
7.1
7.0
6.8/6.5
6.0
5.1
4.8-4.4

Figure 5(B)

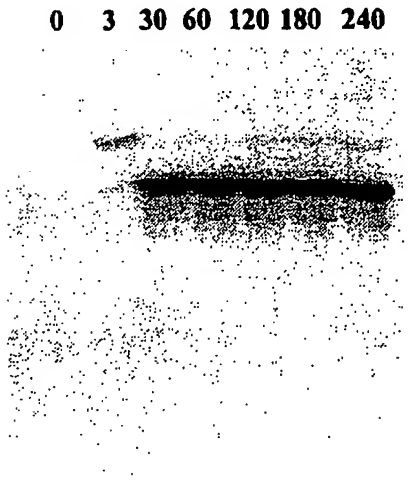


Figure 5(C)

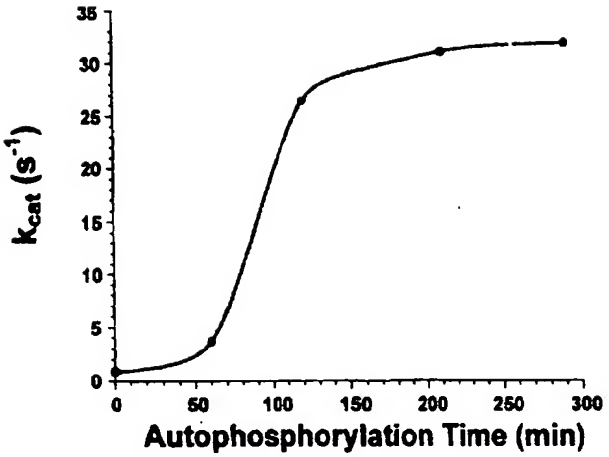
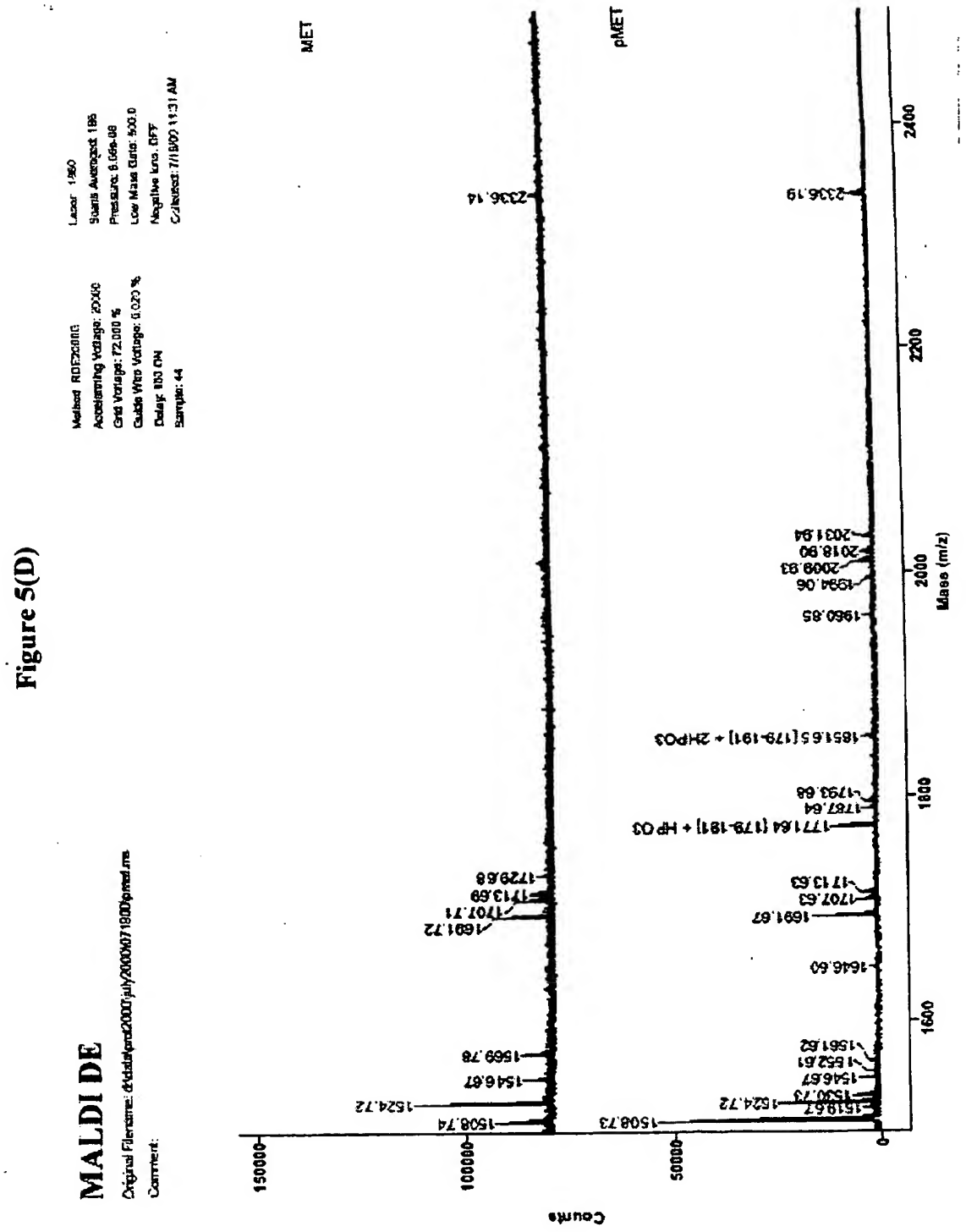

35
30
25
20
15
10
5
0
k_{cat} (s^{-1})
0
50
100
150
200
250
300
Autophosphorylation Time (min)

Figure 5(D)


MALDI DE
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Comment:
Method: RDE2500S
Accelerating Voltage: 25000
Grid Voltage: 72.000 %
Guide Wire Voltage: 0.020 %
Delay: 100 ns
Sample: 44
Laser: 1960
Shots Averaged: 185
Pressure: 6.66e-08
Low Mass Gate: 500.0
Negative Ions: OFF
Collected: 7/19/00 11:31 AM
MET
pMET
1508.74
1524.72
1546.67
1569.78
1691.72
1707.71
1713.69
1729.68
2336.14
1508.73
1524.72
1546.67
1552.61
1561.62
1646.60
1691.67
1707.63
1713.63
1771.64 [179-181] + HPO3
1787.64
1793.66
1851.65 [179-181] + 2HPO3
1960.85
1994.06
2009.83
2018.90
2031.94
2336.19
Counts
Mass (m/z)

Figure 5(E)

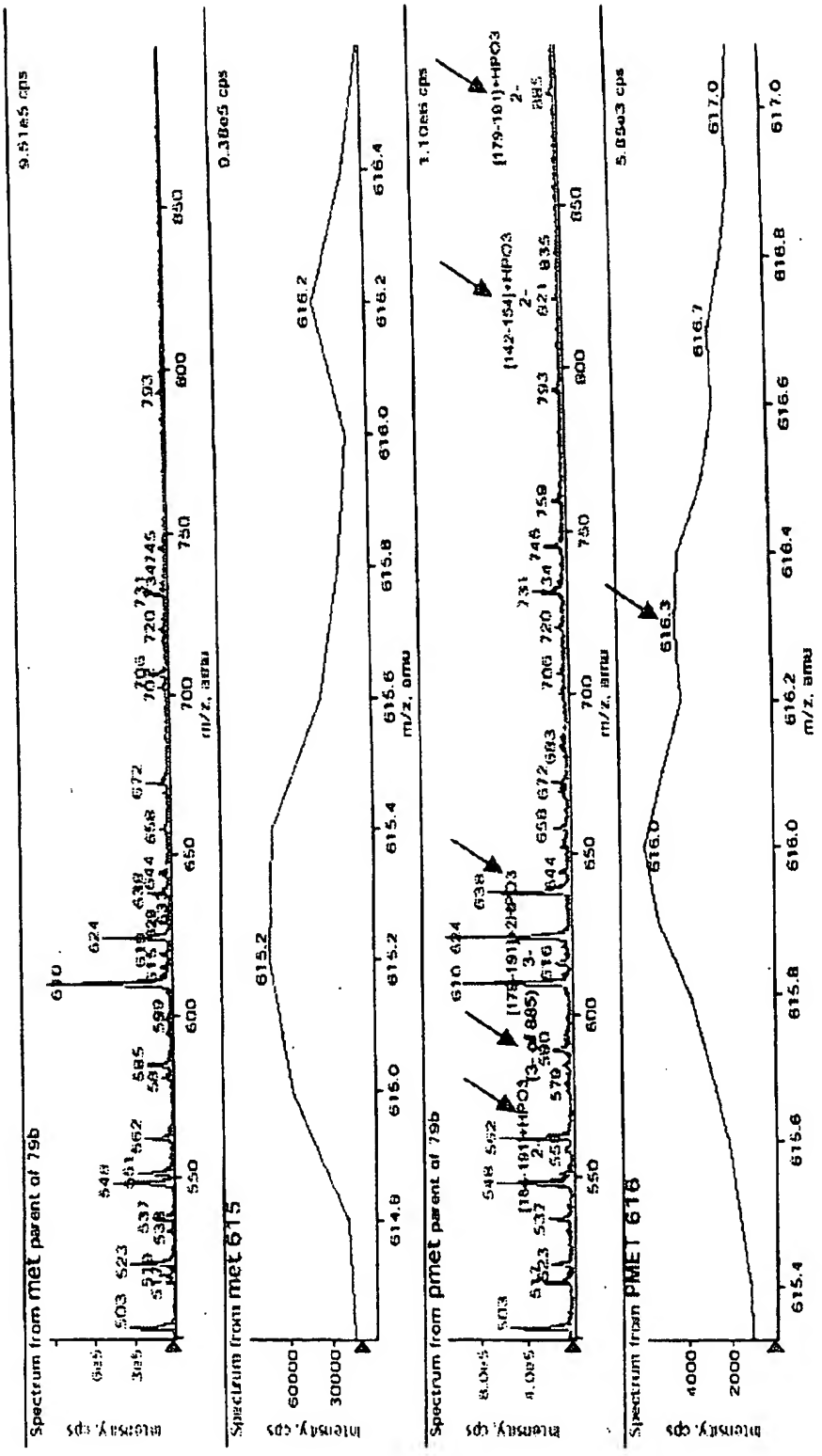

Spectrum from met parent of 79b
Spectrum from met 615
Spectrum from pmet parent of 79b
Spectrum from pMET 616
intensity, cps
m/z, amu
[142-154]+HPO3 2-
[179-191]+HPO3 2-
[179-191]+HPO3 3-
(3-of 885)

Figure 6(A)

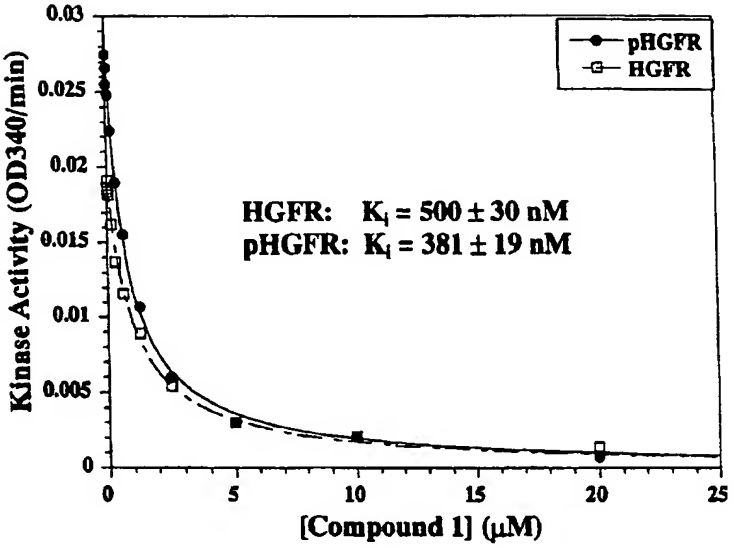
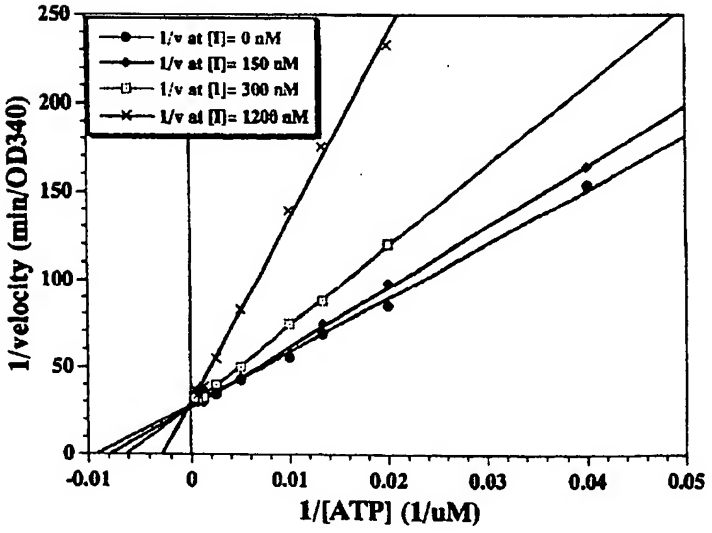


Figure 6(B)



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European Patent Office
Office européen des brevets

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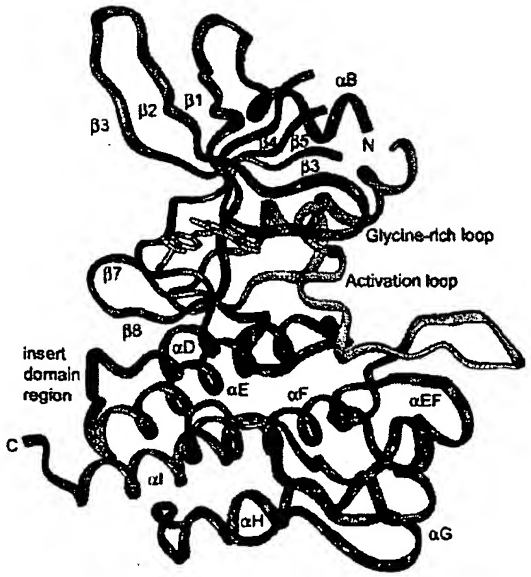
(54) Catalytic domains of the human hepatocyte growth factor receptor tyrosine kinase and methods for identification of inhibitors thereof

(57) The identification, isolation, purification, and characterization of the catalytic domain of the human hepatocyte growth factor receptor kinase (hHGFR) are described. A crystal structure of the hHGFR kinase domain is reported herein. This structure provides a three-dimensional description of the binding site of the hHGFR for structure-based design of small molecule inhibitors thereof as therapeutic agents. The kinase domain of human HGFR and its associated crystal structure is described for use in the discovery, identification and characterization of modulators of human HGFR.

Figure 2



EP 1 243 596 A3

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 02 00 6616

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	LIU YOUHUA: "The human hepatocyte growth factor receptor gene: Complete structural organization and promoter characterization." GENE (AMSTERDAM), vol. 215, no. 1, 17 July 1998 (1998-07-17), pages 159-169, XP004149240 ISSN: 0378-1119 Abstract, discussion * figures 2-5 * --- -/--	1-6, 19-52	C07K14/71 C12N15/12 G01N33/53

TECHNICAL FIELDS SEARCHED (Int.Cl.7)

C07K
C12N
G01N

INCOMPLETE SEARCH

The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.

Claims searched completely :

1-70,73-76

Claims searched incompletely :

Claims not searched :

71,72

Reason for the limitation of the search:

Article 52 (2)(c) EPC - Scheme, rules and method for performing mental acts, re. claims 71 and 72

Place of search	Date of completion of the search	Examiner
MUNICH	18 December 2002	Bretherick, J

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C07)

European Patent Office

Application Number
EP 02 00 6616

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-6, 19-52

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 02 00 6616

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	DATABASE EMBL [Online] EMBL; 100% identity (100.000% ungap) 4620nt overlap, 13 March 1996 (1996-03-13) GREEN E.D.: "Human Chromosome 7-specific STSs" retrieved from EBI Database accession no. G18239 XP002199816 * abstract *	1-6, 19-37, 43,47,48	
X	& BOUFFARD ET AL.: "A collection of 1814 human chromosome 7-specific STSs" GENOME RES., vol. 7, no. 1, 1997, pages 59-64, * the whole document *	1-6, 19-52	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	DATABASE SWISS-PROT [Online] EMBL; 100% Identity with SEQ ID NO. 2, 1 August 1988 (1988-08-01) GIODANO, S.: "Hepatocyte Growth Factor Receptor Precursor (EC 2.7.1.112)" retrieved from EBI Database accession no. P08581 XP002199817 * abstract *	1-6, 19-37, 43,47,48	

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EPO FORM 1503 03.82 (P04C10)

European Patent Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 02 00 6616

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-6,19-52

An isolated polynucleotide which encodes the human hepatocyte growth factor receptor, catalytically active form thereof,or the human hepatocyte growth factor receptor kinase domain,or a fragment or variant thereof, isolated polypeptides encoded by said polynucleotides, soluble polypeptides, expression vectors, hosts, methods of producing said polypeptides

2. Claims: 7-18, 53-61, 64-70, 73-76

A crystal structure comprising the human hepatocyte growth factor receptor kinase, Method for assaying a candidate compound for its ability to interact with the human hepatocyte growth factor receptor involving crystalisation of said kinase in a condition suitable for x-ray crystallography, use of results thereof, processes of drug design involving x-ray crystallography of kinase, methods of assessing compounds which are agonists or antagonists involving x-ray crystallography and/or the results obtained therefrom, methods of determining the 3-dimensional structure of a complex of hepatocyte growth factor with a ligand thereof, use of same in a drug discovery strategy, computers and data storage devices containing various coordinate information according to table 1 and capable of, inter alia, producing a 3-dimensional representation of the hepatocyte growth factor kinase amino acids.

3. Claims: 62, 63

Method of rapidly screening large compound libraries to identify compounds that inhibit human hepatocyte growth factor receptor kinase, comprising a non-radioactive immunosorbent assay capable of robotic control, for example DELFIA.

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 02 00 6616

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	FERRACINI R ET AL: "IDENTIFICATION OF THE MAJOR AUTOPHOSPHORULATION SITE OF THE MET/HEPATOCYTE GROWTH FACTOR RECEPTOR TYROSINE KINASE*" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 266, no. 28, 15 October 1991 (1991-10-15), pages 19558-19564, XP000941367 ISSN: 0021-9258 Abstract, discussion, Figs. 1-11 ---	1-6, 19-52	
X	BOTTARO D P ET AL: "IDENTIFICATION OF THE HEPATOCYTE GROWTH FACTOR RECEPTOR AS THE C-MET PROTO-OCOGENE PRODUCT" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 251, 15 February 1991 (1991-02-15), pages 802-804, XP000941505 ISSN: 0036-8075 * the whole document * ---	1-6, 19-52	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
A	LOKKER NATHALIE A ET AL: "Generation and characterization of a competitive antagonist of human hepatocyte growth factor HGF/NK1." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 268, no. 23, 1993, pages 17145-17150, XP000942254 ISSN: 0021-9258 * the whole document * ---		
	-/--		

EPO FORM 1503 03.82 (P04C10)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 02 00 6616

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	LOKKER N A ET AL: "STRUCTURE-FUNCTION ANALYSIS OF HEPATOCYTE GROWTH FACTOR: IDENTIFICATION OF VARIANTS THAT LACK MITOGENIC ACTIVITY YET RETAIN HIGH AFFINITY RECEPTOR BINDING" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 11, no. 7, 1 July 1992 (1992-07-01), pages 2503-2510, XP002036379 ISSN: 0261-4189 * the whole document * ---		
A	EP 0 520 158 A (ERBA CARLO SPA) 30 December 1992 (1992-12-30) * claims 1-4; example 1 * -----		TECHNICAL FIELDS SEARCHED (Int.Cl.7)

EPO FORM 1503 03.82 (P04C10)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 02 00 6616

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
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18-12-2002

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0520158 A	30-12-1992	AT 155525 T	15-08-1997
		AU 651452 B2	21-07-1994
		AU 1672092 A	30-12-1992
		CA 2102595 A1	11-11-1992
		DE 69220940 D1	21-08-1997
		DE 69220940 T2	15-01-1998
		DK 584125 T3	08-09-1997
		WO 9220792 A1	26-11-1992
		EP 0520158 A1	30-12-1992
		EP 0584125 A1	02-03-1994
		ES 2104914 T3	16-10-1997
		FI 934934 A	05-01-1994
		GR 3024998 T3	30-01-1998
		HU 67009 A2	30-01-1995
		IE 921485 A1	18-11-1992
		JP 6508508 T	29-09-1994
		JP 3293823 B2	17-06-2002
		MX 9202129 A1	01-11-1992
		NZ 242645 A	25-11-1994
		RU 2124024 C1	27-12-1998
		US 5571509 A	05-11-1996
		ZA 9203342 A	27-01-1993

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82